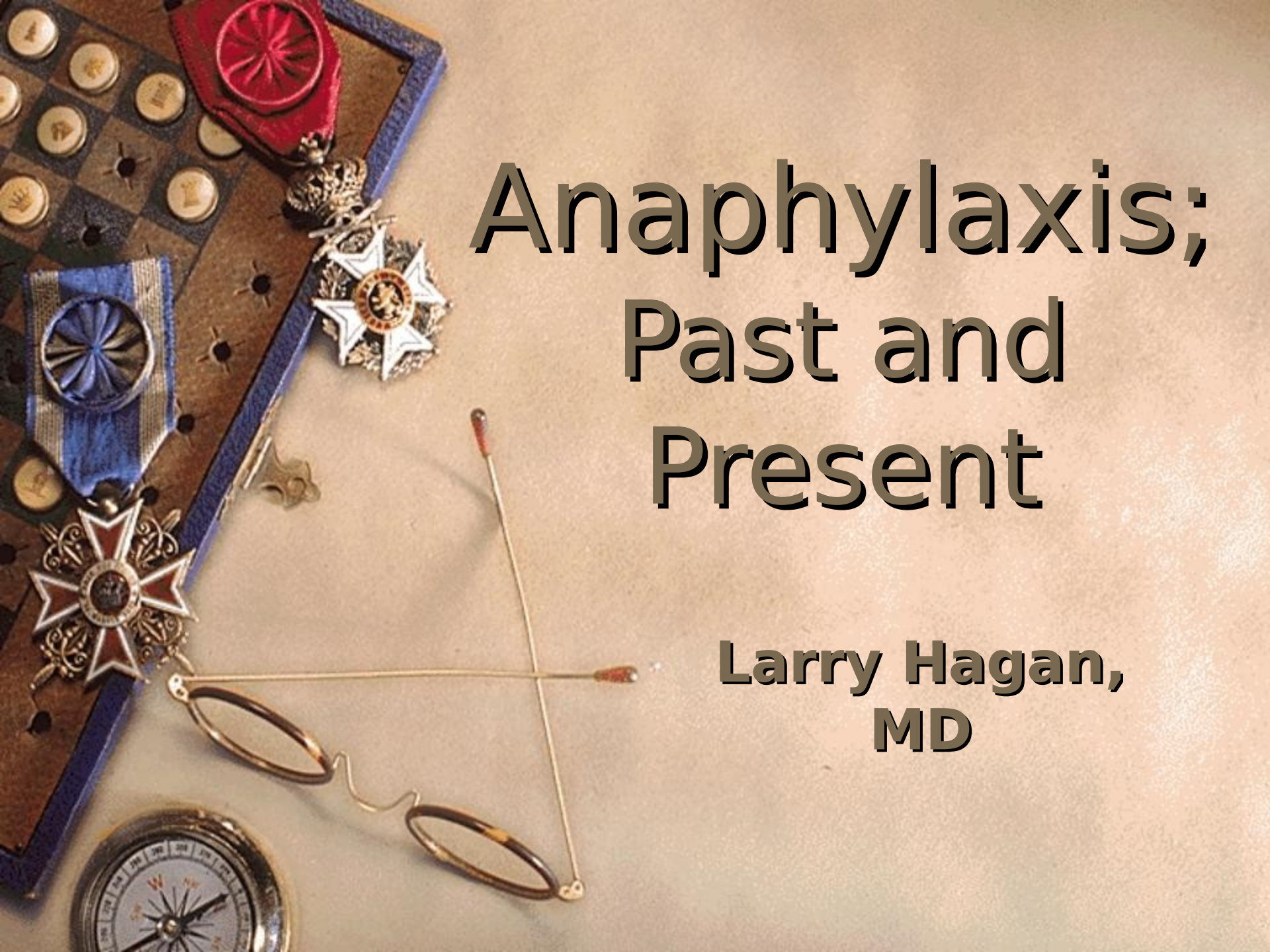
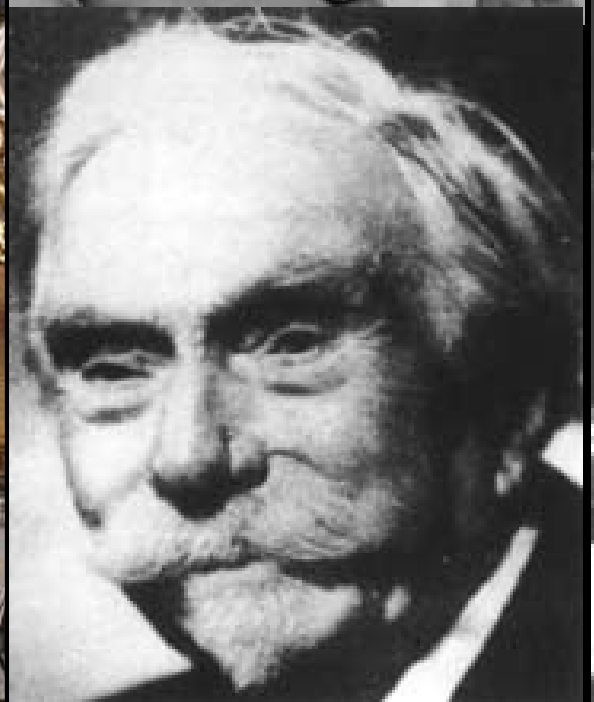
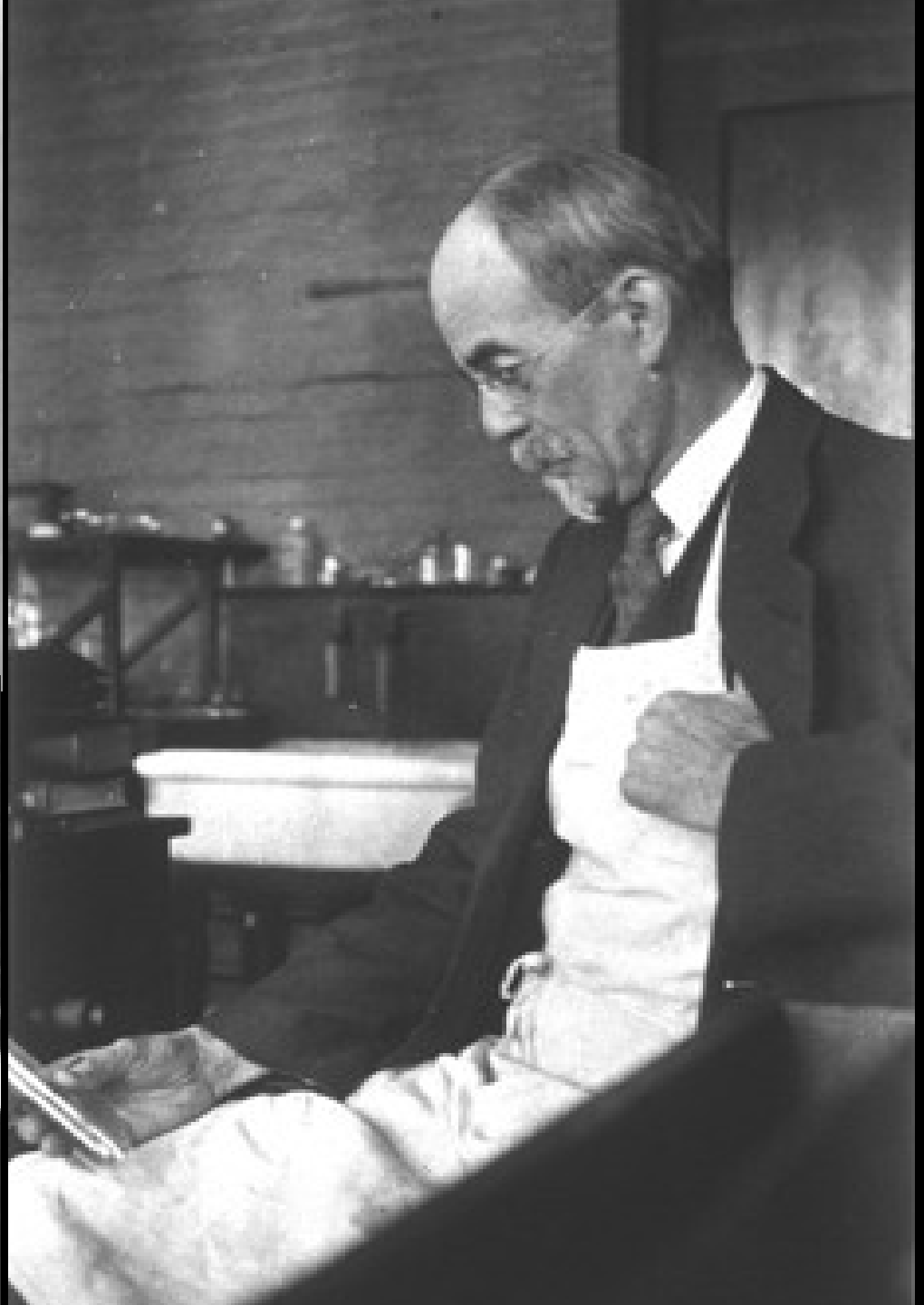


Anaphylaxis; Past and Present

Larry Hagan, MD

King Menses of Egypt





100 Years of Anaphylaxis: 1902-2002

Animal Reports

- Magendie:
  egg albumen in **1839**
- Behring:
  diphtheria toxin **1893**
- Flexner:
  dog serum in **1894**
- Richet:
  toxic eel serum **1898**

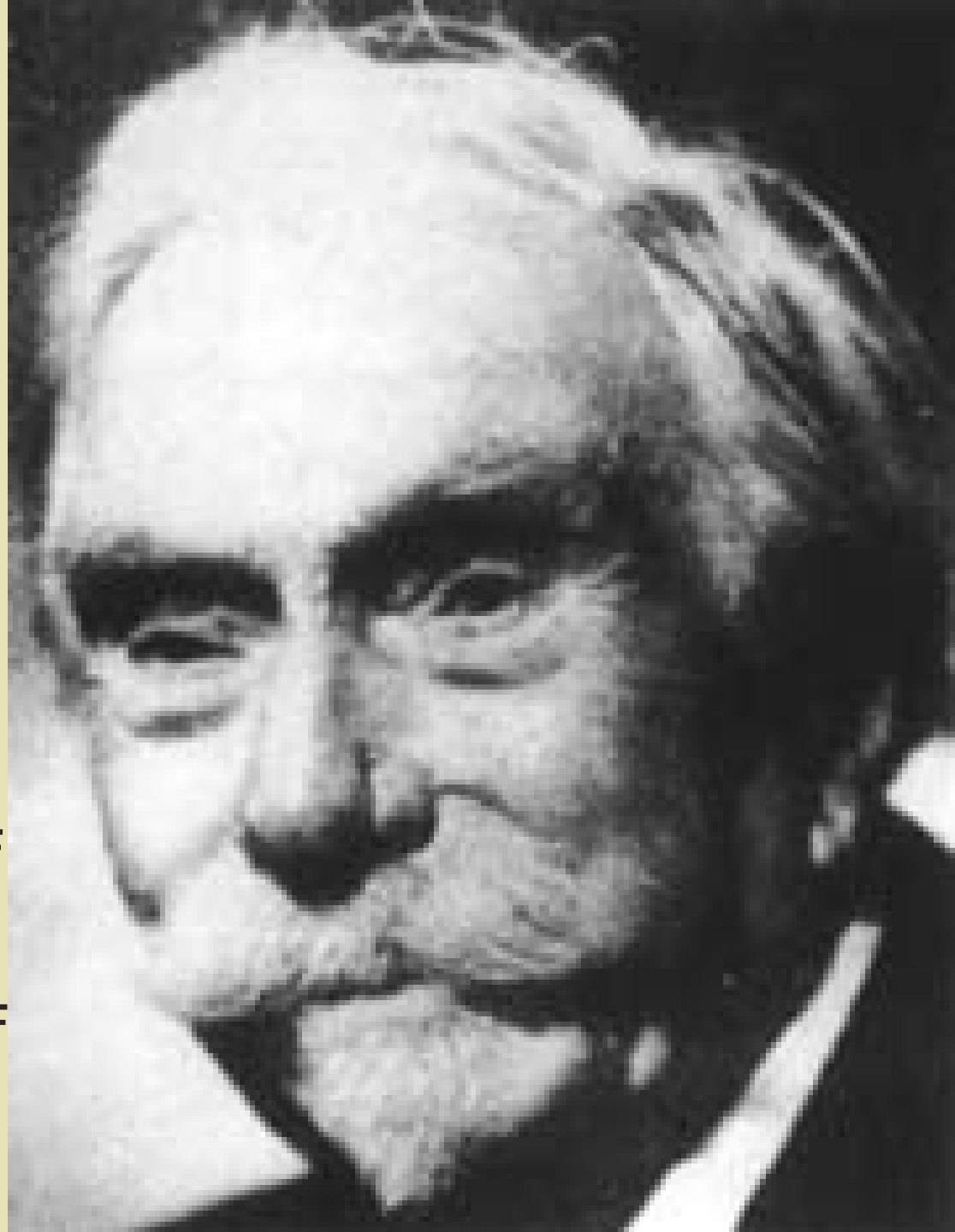
Anaphylaxis in Humans

- Gottstein: **1896**
- Reported 7 human fatalities to the administration of horse-derived Diphtheria antisera
- “Incidental findings”

Albert Grimaldi

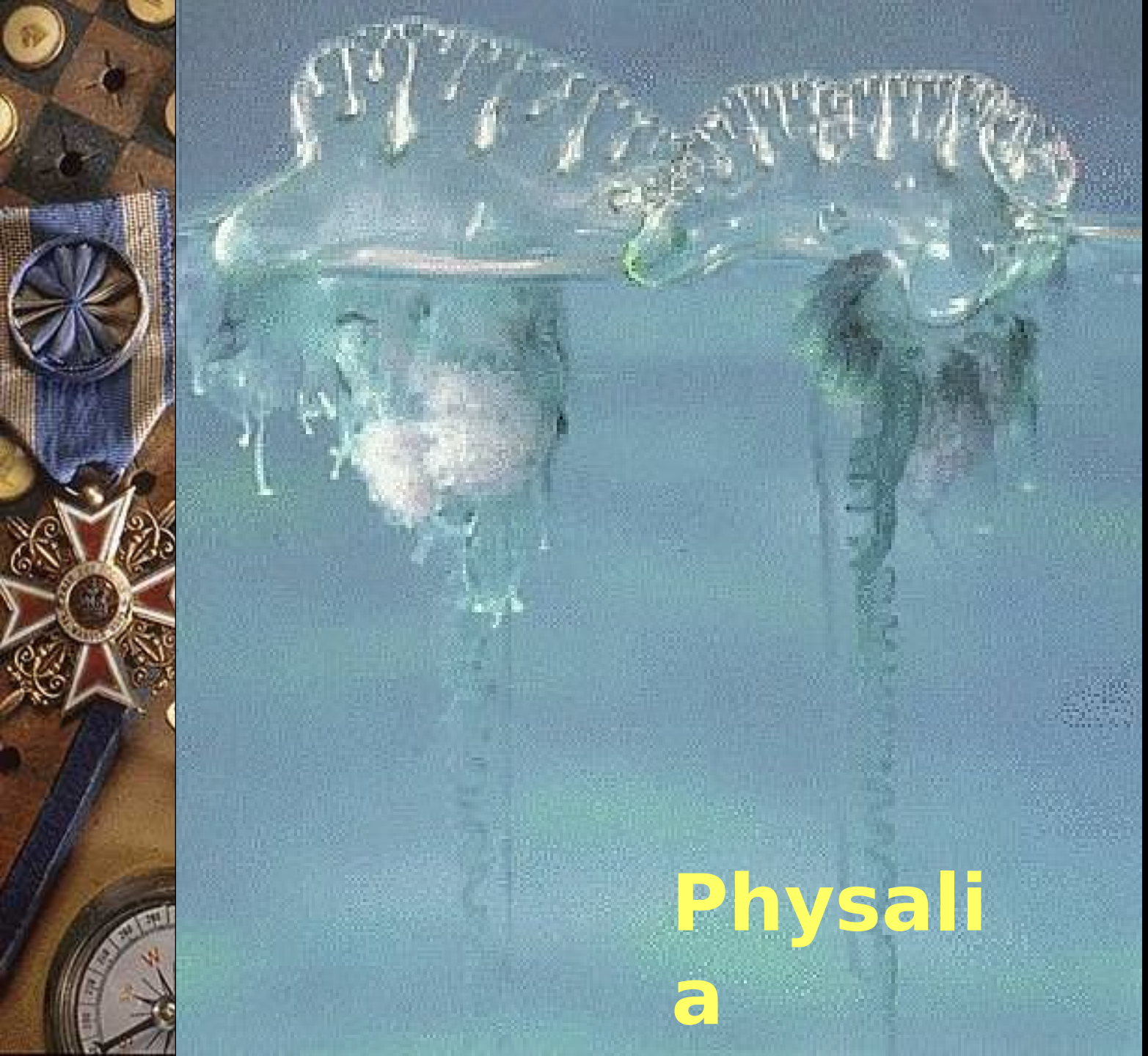
Paul Portier

Assistant in the University of Paris' laboratory of physiology



Charles Richet

- Digestion
- Thermal regulation
- Respiratory control
- Aircraft
- Poisons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Hypnotox
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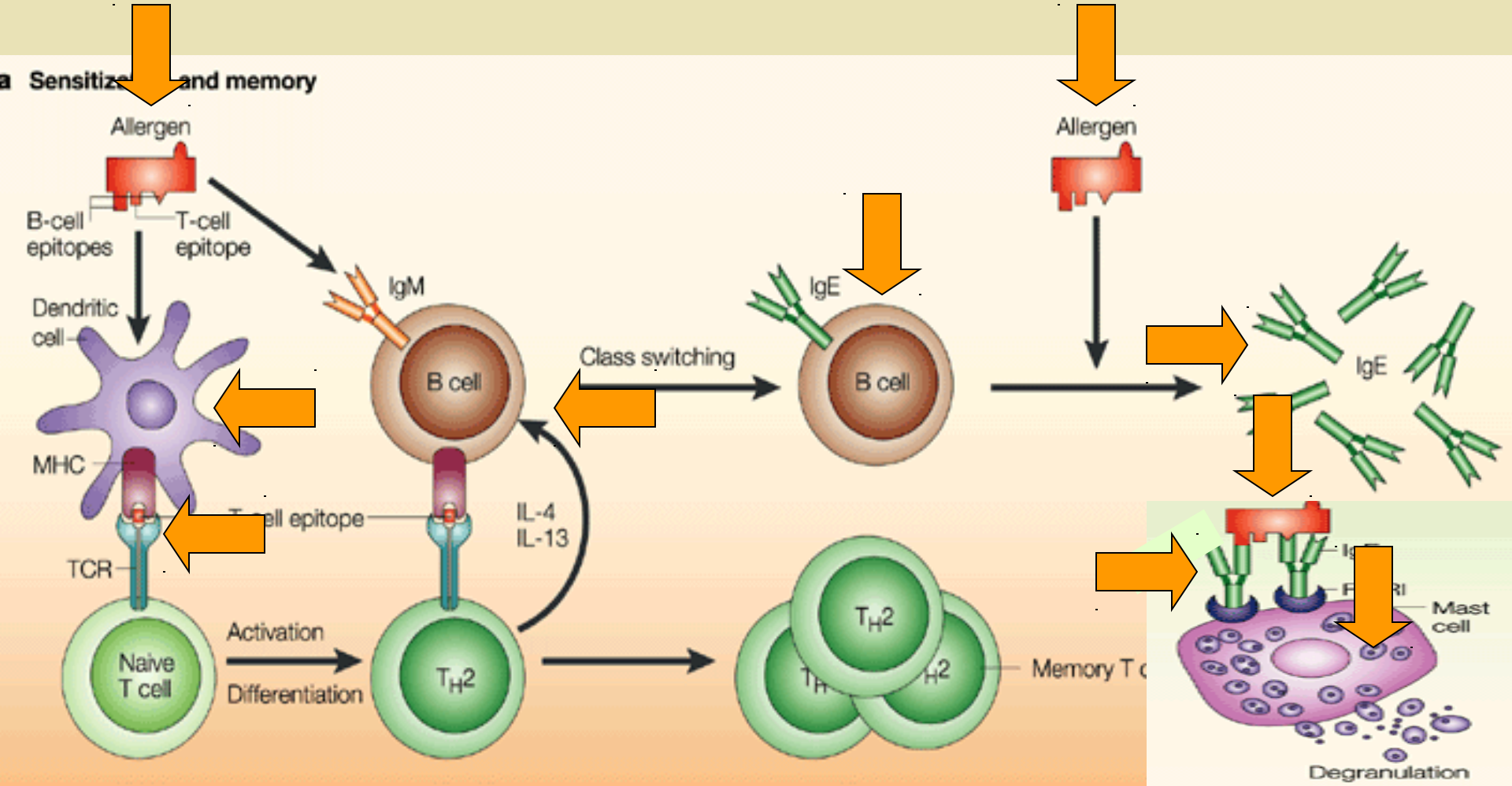
Induced Tolerance?

- *Question*: "Can repeated injections of increasing amounts at set intervals induce tolerance to the toxin?"
- 8 dogs who had previously received injections several weeks earlier, collapsed and died within a few minutes after repeat administration of a small dose of the toxin

- ***Richet and Portier*** : a development of a sensitive state seemed to correlate with having ***"received the first injection at a remote date"***



Galathée and Neptune

- Previously received 2 doses of the toxin
- Injected with “weaker doses”
- Itching, dyspnea, vomiting blood and mucus, marked stupor, and death
- *“Administration of a substance insufficient to kill or even sicken a normal animal … produces fulminating symptoms and death in an animal previously inoculated with the same substance.”*

“Anaphylaxis”

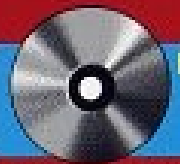
- Richet proposed the name “aphylaxis” (derived from the Greek words a- (against) and -phylaxis (protection)
- Changed to “anaphylaxis” because it was more euphonic

- Richet received the Nobel prize in Medicine or Physiology

- Portier was not included as a recipient

Oceanographic Institute and Museum

1906



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DEFINITIONS OF ANAPHYLAXIS AND ANAPHYLACTOID EVENTS

- **Anaphylaxis**
  - Immediate systemic reaction
  - IgE-mediated
  - Mediators from mast cells and basophils
- **Anaphylactoid** reactions
  - Not IgE-mediated
  - Cytotoxicity or immune complex mediated
  - Mast cell or basophil degranulation

ANAPHYLAXIS vs. ANAPHYLACTOID

- Anaphylaxis
  - Penicillin
  - Foods
  - Venoms
  - Latex
- Anaphylactoid
  - Blood transfusion
  - Gammaglobulin administration
  - Radiocontrast media
  - ASA sensitivity
  - Vancomycin (Red Man Syndrome)

Demographics

- Anaphylaxis is not reportable
- 84,000 cases of anaphylaxis and 840 deaths annually in USA[1]
- 154 cases/1 million hospitalizations internationally[2]

1. JACI 1999;104:452

2. Epidemiology1998;9:141

Symptoms

- Commonly occur within a few seconds or minutes
- ***Sometimes*** the onset of symptoms can be delayed for several hours
- The more rapidly symptoms ensue, the more severe the reaction

Symptoms

- Erythema, flushing or pruritus
- Urticaria and angioedema
- Nasal, ocular, and palatal pruritus
- Sense of impending doom
- Gastrointestinal symptoms
- Uterine cramps
- Dizziness, syncope, loss of consciousness
- Hypotension
- Convulsions

Symptoms

- **Upper airway obstruction**
  - Hoarseness
  - Dysphonia
  - Difficulty swallowing.
- **Lower airway obstruction**
  - Wheezing
  - Chest tightness

What Things Cause Anaphylaxis?

Drugs

β-LACTAM ANTIBIOTICS

- Penicillin responsible for **75%** of anaphylactic deaths in the United States
- **400-800** fatalities per year in USA
- **80%** of patients with a history of allergy to penicillin do **not** have IgE antibodies

β-LACTAM ANTIBIOTICS
Skin Testing

- Identifies patients with IgE antibodies specific for penicillin
- RAST or ELISA testing does not reliably rule out allergy to penicillin
- If skin test results for penicillin with major (penicilloyl) and minor determinants (penicillin G and others) are negative, 97%-99% of patients will tolerate penicillin
- Does not predict the later development of IgE-mediated reactions or non-IgE mediated reactions

β-LACTAM ANTIBIOTICS
Skin Testing

- If a patient has a positive history and a positive skin test, there is a 50% chance of an immediate reaction if penicillin is given again
- The patient should receive an alternative antibiotic
- If administration of penicillin is mandatory in this setting, desensitization is indicated

Aspirin & NSAIDS

ASA/NSAIDS
Types of Reactions

- **Urticaria**
- **Angioedema**

ASA/NSAIDS Types of Reactions

- Rhinoconjunctivitis
- Bronchospasm
- Prostaglandin inhibition

- Anaphylaxis
  - IgE mediated

ASA / NSAIDS: Diagnosis and Therapy

- No definitive skin or in vitro test to identify patients who are intolerant to ASA or NSAIDs.
- Diagnosis: Oral challenge
- Therapy: Desensitization

Foods
THAT WASN'T CHICKEN

Foods

- 150 fatalities/year
- Anaphylactic reactions to foods almost always occur immediately
- Symptoms ma

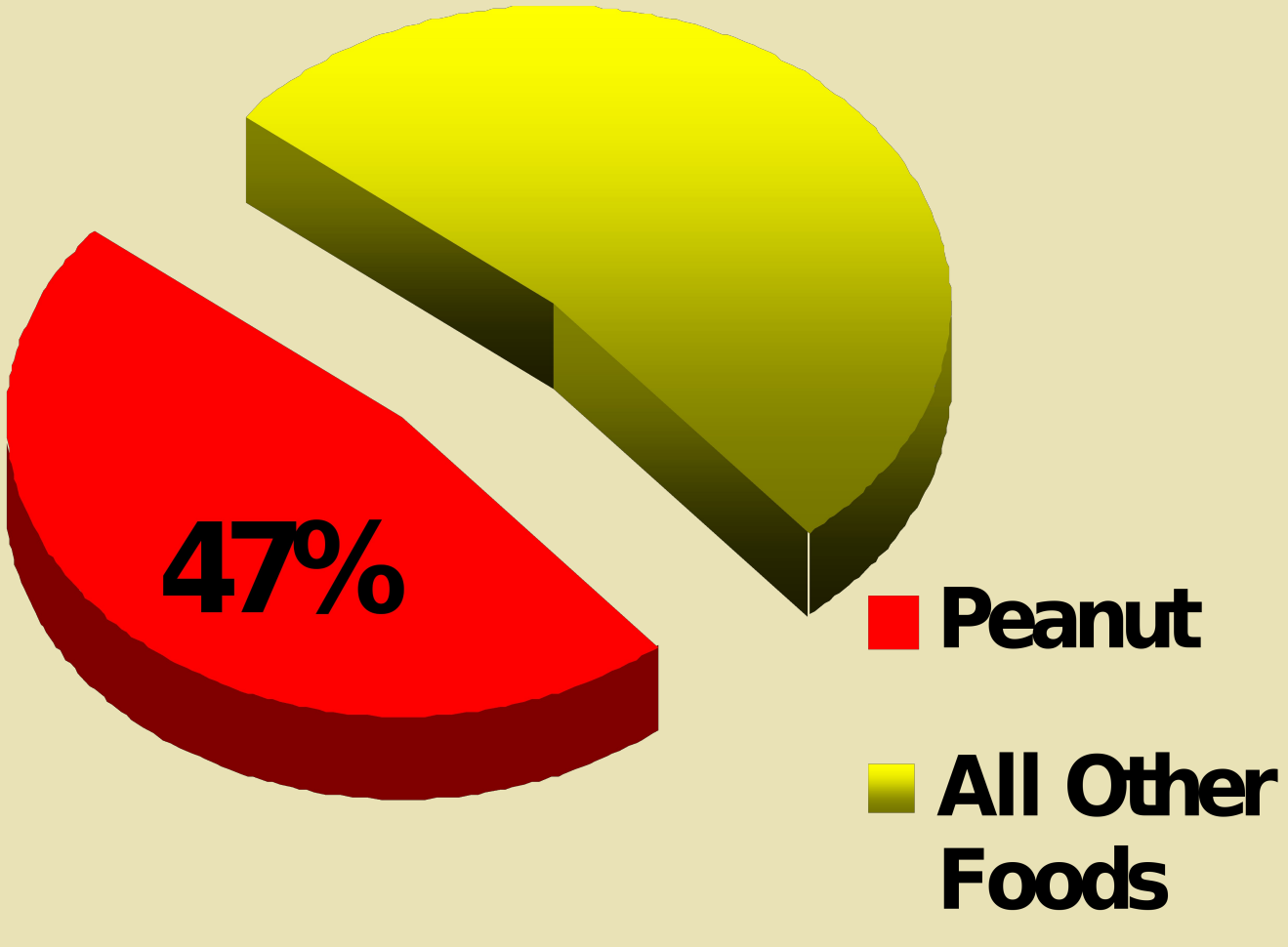
- 94% of fatal anaphylaxis to foods involve peanuts or true nuts*

*** JACI 2001;107:191-3**

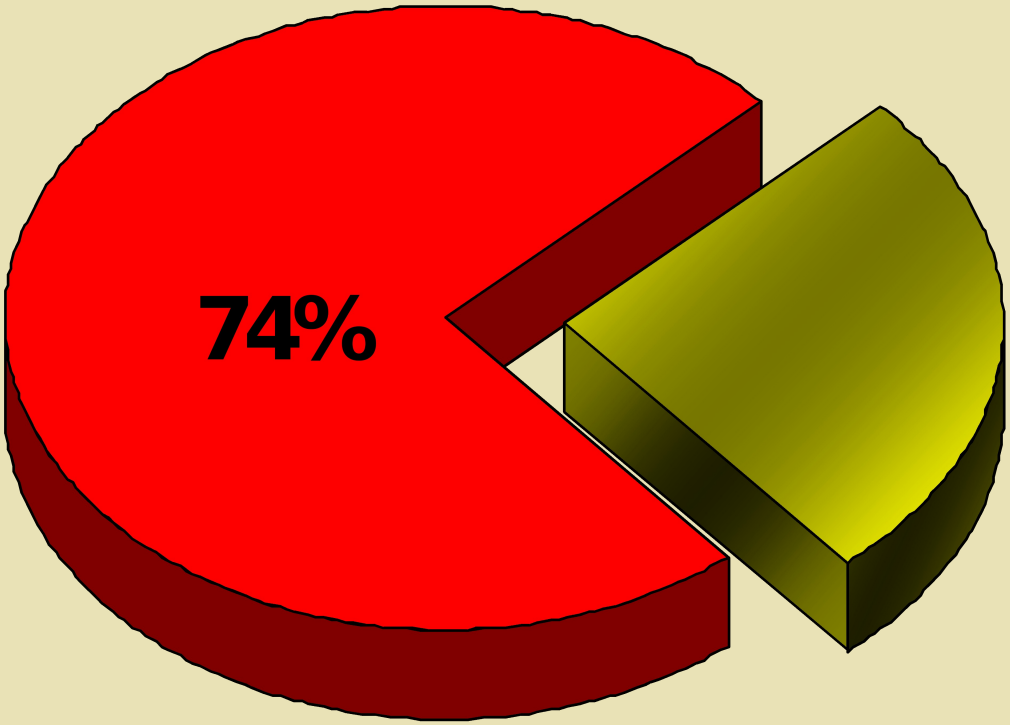
MR. PEANUT

The
PUBLIC
ENEMY
JAMES CAGNEY JEAN HARLOW
EDWARD WOODS JOAN BLONDELL
WILLIAM A. WELLMAN
A WARNER BROS.
VITAPHONE

Anaphylaxis Attributed to Foods

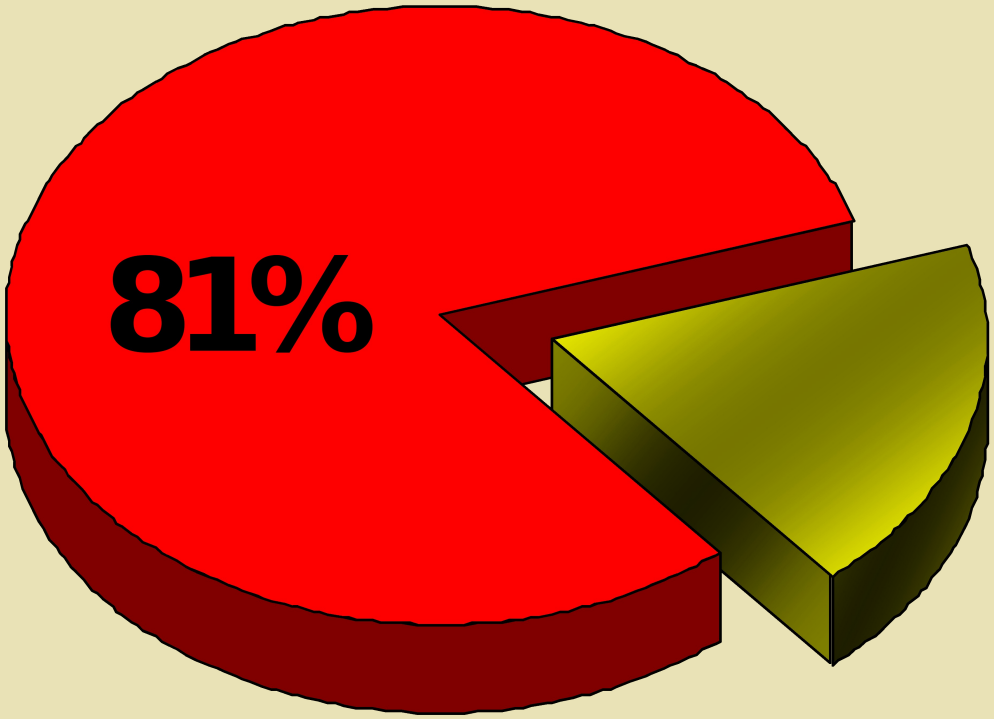


Reactions to Peanut Occurring on the First Known Exposure



Children can be sensitized prenatally and by breast feeding from maternal diet, or from moisturizing lotions containing

Peanut: Severe Anaphylaxis



Arch Allergy Immunology
1999;119:165-172

Fatalities Due To Anaphylaxis To Foods*

- 32 fatal cases from 1994-1999 analyzed
- Peanut accounted for **63%** of fatalities
  - Other nuts: **31%**
- **All** ingestions were **"accidental"**
- **84%** occurred outside of home
- All but 1 had **asthma** (97%)
- Epinephrine was **NOT** given or was given very late in **88%**

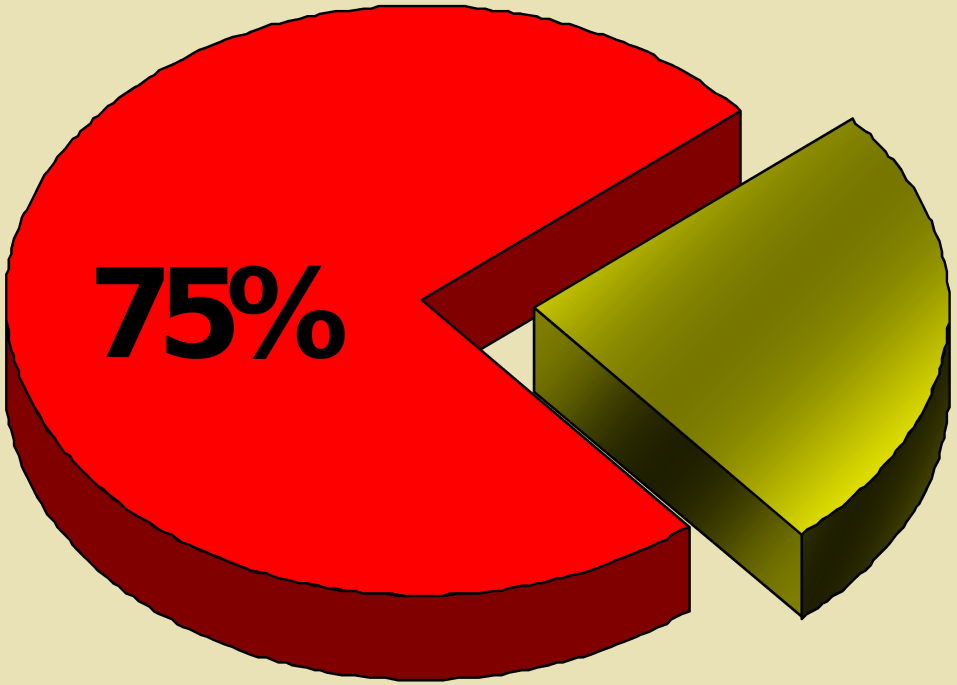
JACI* **2001;107:191-193

Avoidance…Easier Said Than Done

- 25% of labels may not reflect the presence of peanut[1]
- Sensitive patients may react to trace amounts of peanut
- Contact with or inhalation of peanut might occur on airlines[2]
- Most common places:
  - Asian restaurants, bakeries and ice cream shops
  - Desserts

1. **www.cfsan.fda.gov/~dms/alrgpart.html**
2. ***JACI* 1999;104:186-9**

Peanut Reactions Secondary to Accidental Exposures



***J Pediatrics* 2000;137:749-755**

Treatment Strategies for School*

- Written treatment protocols
- Epinephrine readily available (not locked up)
- Education of supervising personnel on:
  - Recognizing signs of an allergic reaction
  - Technique of medication administration
  - Basic first aid and resuscitation

***Annals of Allergy, Asthma & Immunology* 2002;88:350-1**

The Future of Peanut Allergy?

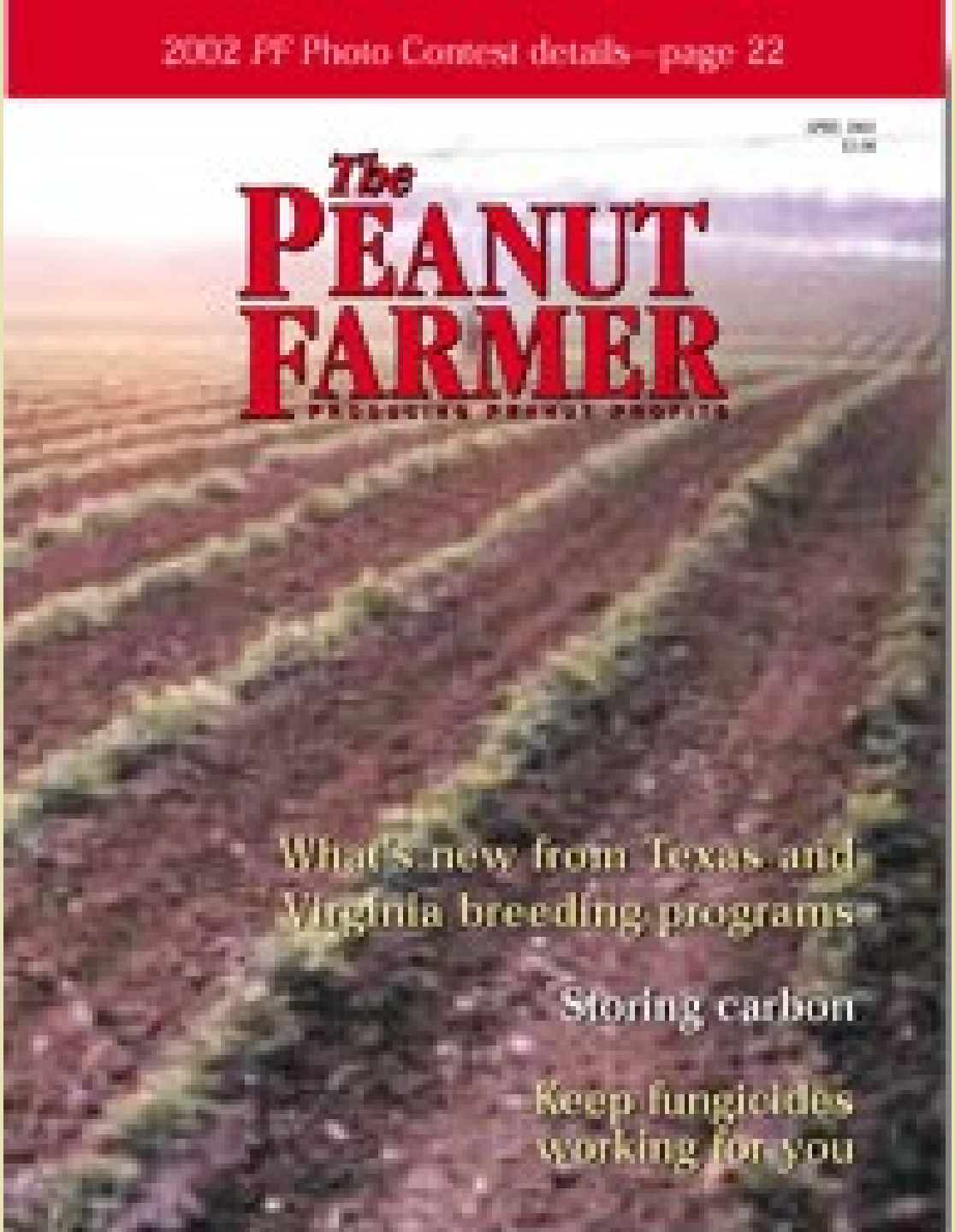
STEVEN SPIELBERG
BACK TO THE FUTURE
A ROBERT ZEMECKIS
"BACK TO THE FUTURE" MICHAEL J. FOX
CHRISTOPHER LLOYD · LEA THOMPSON · CRISPIN GLOVER
ROBERT ZEMECKIS & BOB GALE ALAN SILVESTRI BOB GALE NEIL CANTON
STEVEN SPIELBERG KATHLEEN KENNEDY FRANK MARSHALL
ROBERT ZEMECKIS
MOVIEGODS

Anti-IgE Therapy

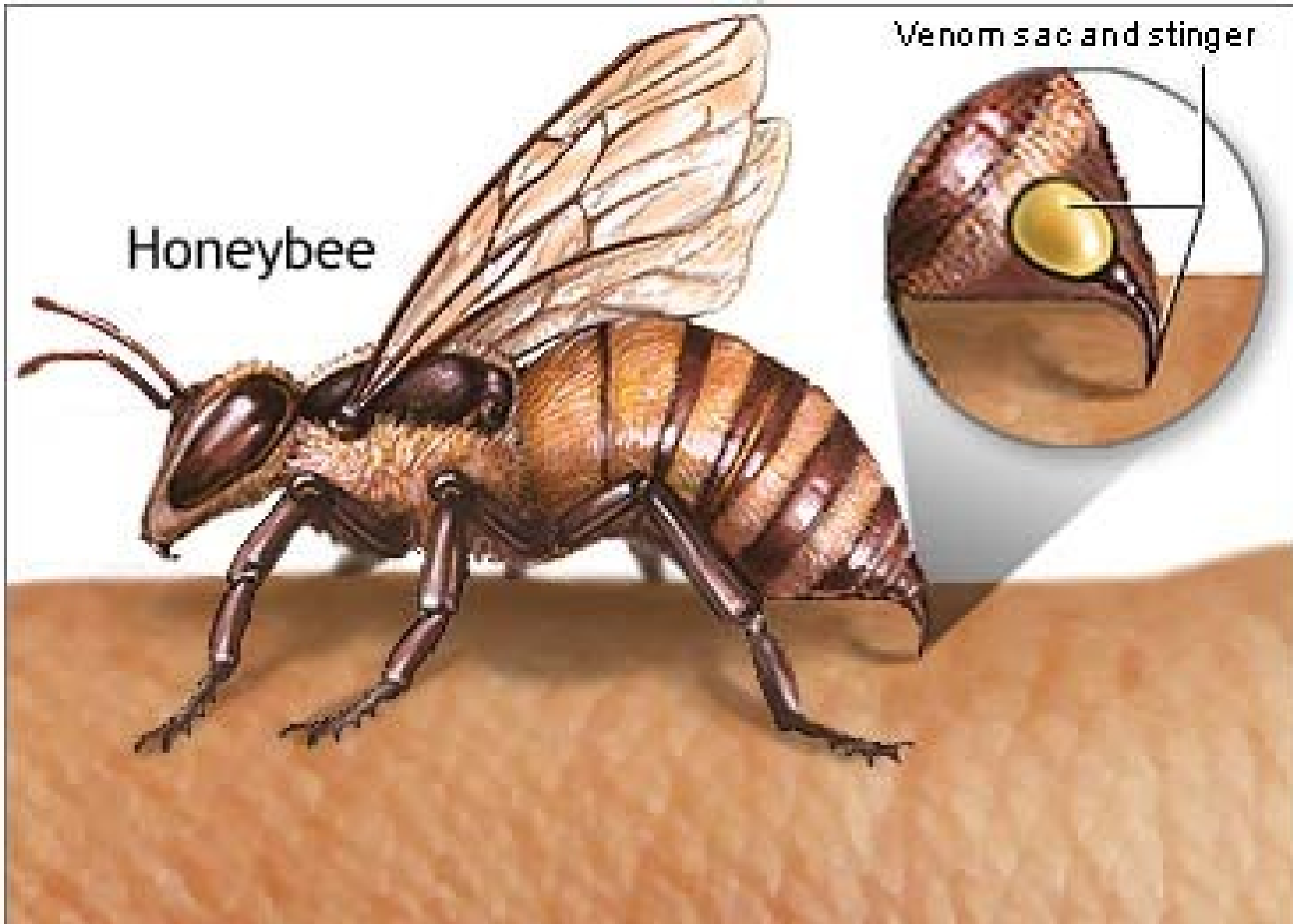
- Increases tolerance up to 9 peanuts*
- Eliminates anaphylaxis from accidental ingestions

***NEJM 2003;348:986-93**

Genetically modified hypoallergenic peanut plant


2002 PF Photo Contest details – page 22
The PEANUT FARMER
What's new from Texas and Virginia breeding programs
Storing carbon
Keep fungicides working for you

INSECT STINGS



Insect Sting Anaphylaxis

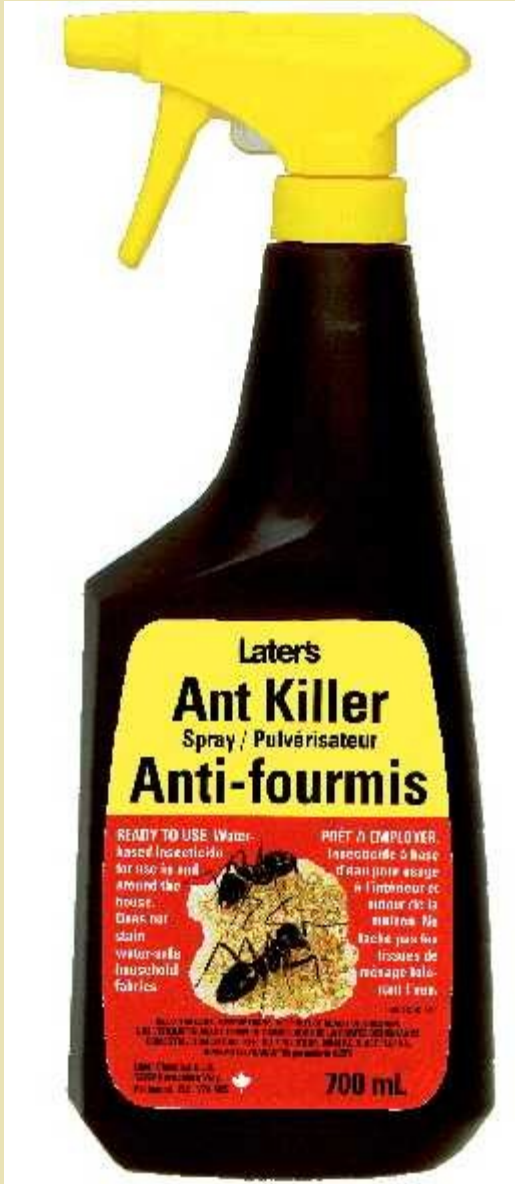
- 50 deaths per year
  - Usually in adults
- Diagnosis: Skin or RAST testing
- 60% chance of recurrence of anaphylaxis when skin test positive

Insect Sting Anaphylaxis
Prevention

- Avoidance
- Don't dress or smell like a flower
- Cover exposed skin
- Insect repellant

Insect Sting Anaphylaxis Prevention

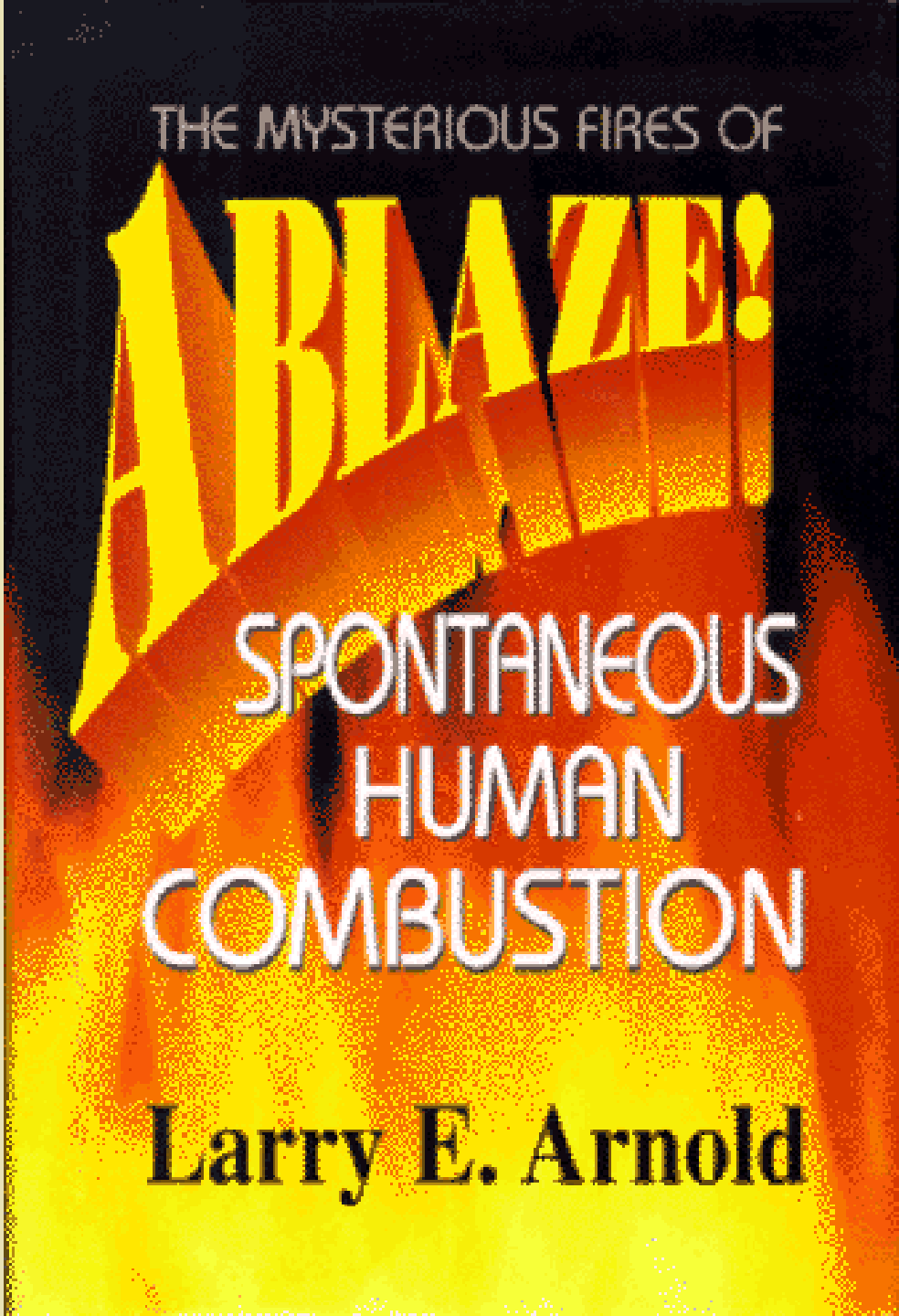
- Kill offending insects



Insect Sting Anaphylaxis Prevention

- Self injectable epinephrine
- Refer to allergist for Immunotherapy
  - ↓ Anaphylaxis risk to 2-3%

Idiopathic Anaphylaxis



Idiopathic Anaphylaxis

- First described in 1978
- Diagnosis of exclusion (foods, venoms, drugs)
- 20,000 - 47,000 patients in the U.S.
- Seen in all ages: The youngest patient reported being 11 months

Idiopathic Anaphylaxis - Classification

- Generalized
- Life-threatening angioedema (upper airway)
- Infrequent
- Frequent (>6 times a year)
- Variants
  - Corticosteroid dependant
  - Malignant (>30mg prednisone/day)
  - Undifferentiated somatoform IA

Idiopathic Anaphylaxis – Autoimmune?*

- 29 patients with IA
- 9 controls
- Flow cytometry for:
  - total lymphocytes
  - CD4 (T-helper cells)
  - CD8 (T-suppressor cells)
  - CD19 (B cells)
  - CD19/CD23 (activated B cells)
  - CD3/HLA-DR (activated T cells)

***Annals of Allergy, 2000;85:368**

Idiopathic Anaphylaxis – Autoimmune?*

- Patients with IA had:
  - Activated T cells
  - More B cells
  - More activated B cells
- Suggestive of immunologic cell activation and an immunologic etiology

***Annals of Allergy, 2000;85:368**

Idiopathic Anaphylaxis Acute Therapy

- Acute episodes
  - **Epinephrine (Epi-Pen)**
  - H1 And H2 blockers
  - Prednisone
  - Go to the nearest Emergency Department

Idiopathic Anaphylaxis Chronic Management (Frequent)

- *Always steroid responsive*
- Prednisone
  - 60 mg/day until symptoms controlled then
  - 80 mg QOD tapered over 6-12 months
- Albuterol 2 mg tid
- H1 blocker
- Prognosis is generally good

Like idiopathic anaphylaxis … but with sweat

Exercise-induced Anaphylaxis Symptoms

- 34,000 individuals in the United States
- Unique form of physical allergy
- Distinct from cholinergic urticaria and exercise-induced asthma

Frequency of EIA Symptoms in 279 Subjects*

- **Pruritus 92%**
- **Urticaria 86%**
- **Angioedema 72%**
- **Flushing 70%**
- **SOB 51%**
- **Dysphagia 34%**
- **Chest tightness 33%**
- **LOC 32%**
- **Diaphoresis 32%**
- **Headache 28%**
- **Nausea/diarrhea/colic 28%**
- **Choking/throat constriction/hoarseness 25%**

*J Allergy Clin Immunol 1999;104:12

Exercise-induced Anaphylaxis Associations

- Atopic history
- Medications
  - Aspirin / other nonsteroidal antiinflammatory agents
- Food ingestion before exercise
  - Eating before exercise
  - Eating specific food before exercise

Transglutaminase-mediated cross-linking of omega-5 gliadin enhances IgE reactivity in wheat-dependent EIA*

- Activation of tissue transglutaminase occurs during exercise in the intestinal mucosa
- Tissue transglutaminase cross-links digested omega-5 gliadin peptides lead to the formation of large allergen complexes
- These cross-linked aggregates bind IgE antibodies more intensely

*Journal of Allergy & Clinical Immunology. 111(6):1386-92

Exercise-induced Anaphylaxis Treatment

- Prophylactic medications not useful
- For food associated symptoms: avoid eating 4 to 6 hours prior to exercise
- Avoid aspirin / NSAIDs before exercise
- EpiPen
- Medic Alert
- Exercise with a partner skilled with EpiPen
- Discontinued exercise at the onset of symptoms

The natural history of exercise-induced anaphylaxis: Survey results from a 10-year follow-up study*

- Analysis of 671 individuals with exercise-associated symptoms followed for a decade
- **46%** stabilized
- **47%** had decreased attacks
- **41%** subjects reported being completely free of attacks in the past year

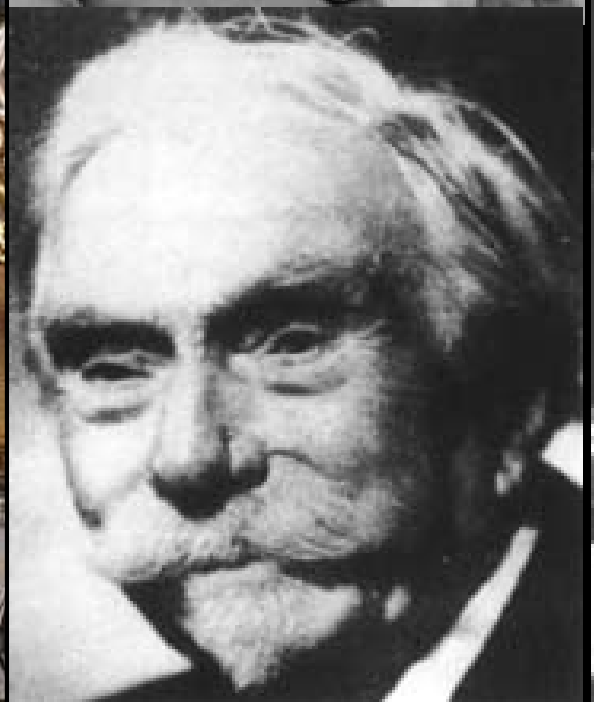
***J Allergy Clin Immunol 1999;104:123**

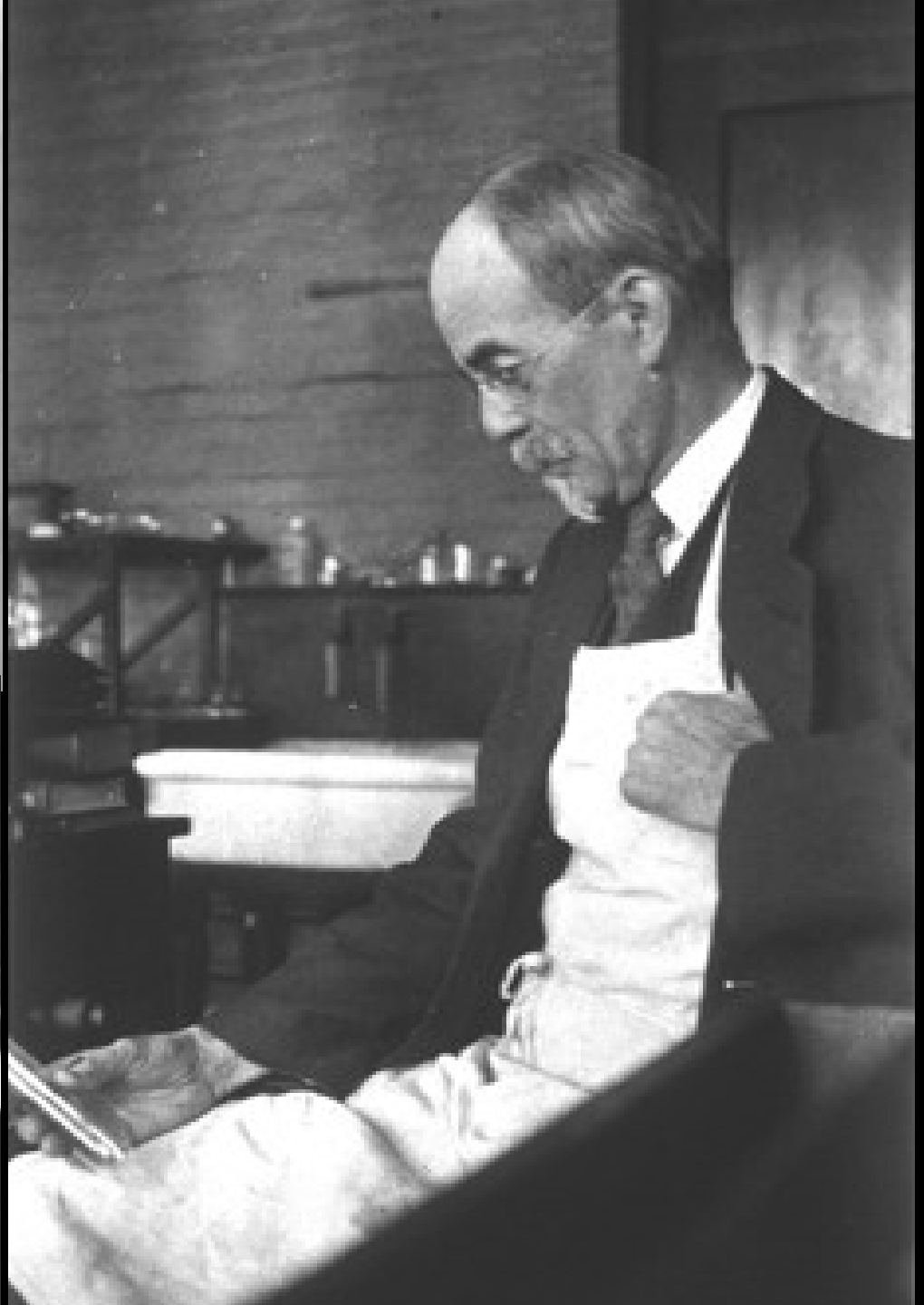
Allergy Shots

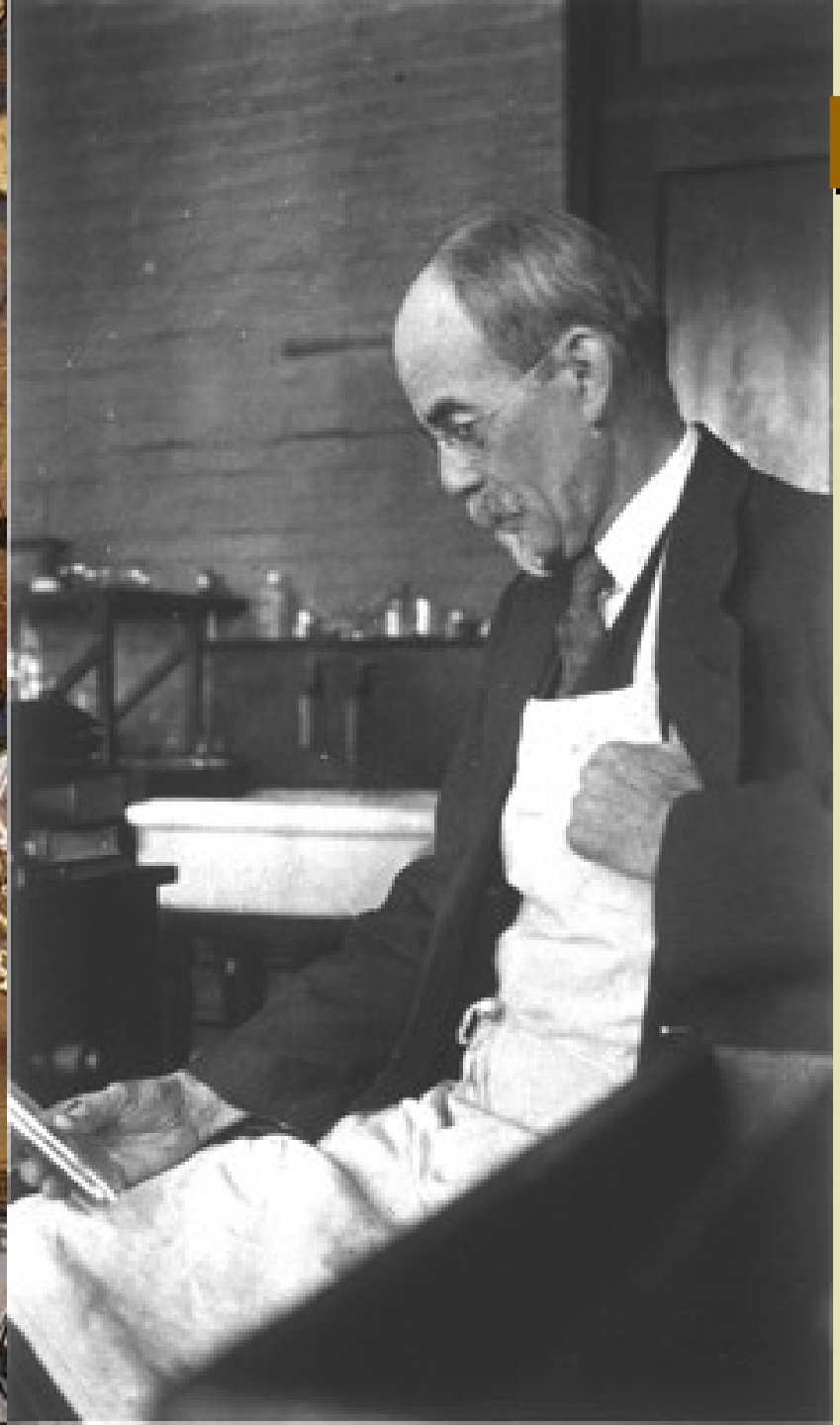
Anaphylaxis : Immunotherapy

- **1929** – Lamson described a death from anaphylaxis after immunotherapy
- Not an infrequent event with ITX
  - **15%** of patients on ITX have anaphylaxis
- Deaths occur (~ 1/year in US)
  - 46 in US from 1945 to 1984
  - 10 in US from 1991 to 1992

Therapy of Anaphylaxis







Epinephrine

John Jacob Abel (18571958)

Epinephrine
Position Statement*
Joint Council of Allergy, Asthma, & Immunology

- Drug of choice
- Dosage
  - Adult: 0.2 ml to 0.5 ml of a 1:1000 dilution SQ or **IM**
  - Children: 0.01 ml/kg, maximum of 0.5 ml
- Repeated every 10 to 15 minutes

***JACI 1998;101:S469**

Effects Of Epinephrine

- Alpha receptor activity
  - Decrease mucosal edema
  - Decreases peripheral vasodilation
  - Decreases vascular permeability
- Beta receptor activity
  - Pulmonary bronchodilation
  - Increase myocardial contractility
  - Suppress release of mediators: histamine, leukotrienes

- Increases blood pressure
- Enhances coronary blood flow
- Improves ventilation and oxygenation

Other Medications

- H1 receptor antagonist (Diphenhydramine)
  - 1 to 2 mg/kg or 25 to 50 mg/dose parenterally
- H2 receptor antagonist
  - Ranitidine (Zantac)
  - When combined with an H1 type may be useful in reversing hypotension refractory to epinephrine and intravascular fluid replacement
  - Adult Dose: 50 mg/dose IV/IM q6-8h

Other Medications

- Glucagon
  - 3-5 mg IM
  - Maintains blood pressure independent of adrenergic receptors by increasing intracellular levels of cyclic AMP
  - Stimulates release of endogenous catecholamines

Other Medications

- Corticosteroids
  - 200 mg hydrocortisone IV
  - *Efficacy of corticosteroids in acute anaphylaxis or in reducing a late anaphylactic reaction has not been clearly established*

Epinephrine is Underutilized

- Friesen et al reviewed 886 charts from a university pediatric ER and a regional university ER from 1994-2001
- 44% of kids and 47% of adults were given epinephrine for anaphylaxis

Epinephrine is Underutilized

- In a study of 78 senior housestaff, 55% did not know how epi was given
- Only 5% knew both the correct route and dose

There are lots of Questions about treatment with Epinephrine

When to Give Epinephrine?

Epinephrine fails to hasten hemodynamic recovery in fully developed canine anaphylactic shock*

- Anaphylaxis in ragweed sensitized dogs
- Epinephrine administered at maximal hypotension
- I.V. vs I.M. vs S.Q.

***International Archives of Allergy and Immunology 2002;128(2):151-164**

Epinephrine fails to hasten hemodynamic recovery in fully developed canine anaphylactic shock*

- Higher plasma concentrations seen in I.V. and I.M.
- Sustained benefit not seen once cardiovascular collapse is fully developed

***International Archives of Allergy and Immunology 2002;128(2):151-164**

Fatal and near-fatal anaphylactic reactions to food in children and adolescents*

- 13 children with anaphylaxis to food
- All with known food allergies
- 6 died
- 7 intubated

***Sampson, NEJM 1992;327:380-4**

Fatal and near-fatal anaphylactic reactions to food in children and adolescents*

- 6 fatal
  - Only 2 had epinephrine in first hour
    - 25 and 60 minutes
- 7 non-fatal
  - 7/7 received epinephrine within 30 minutes

***Sampson, NEJM 1992;327:380-4**

When to Give Epinephrine?

ASAP

after the onset of symptoms

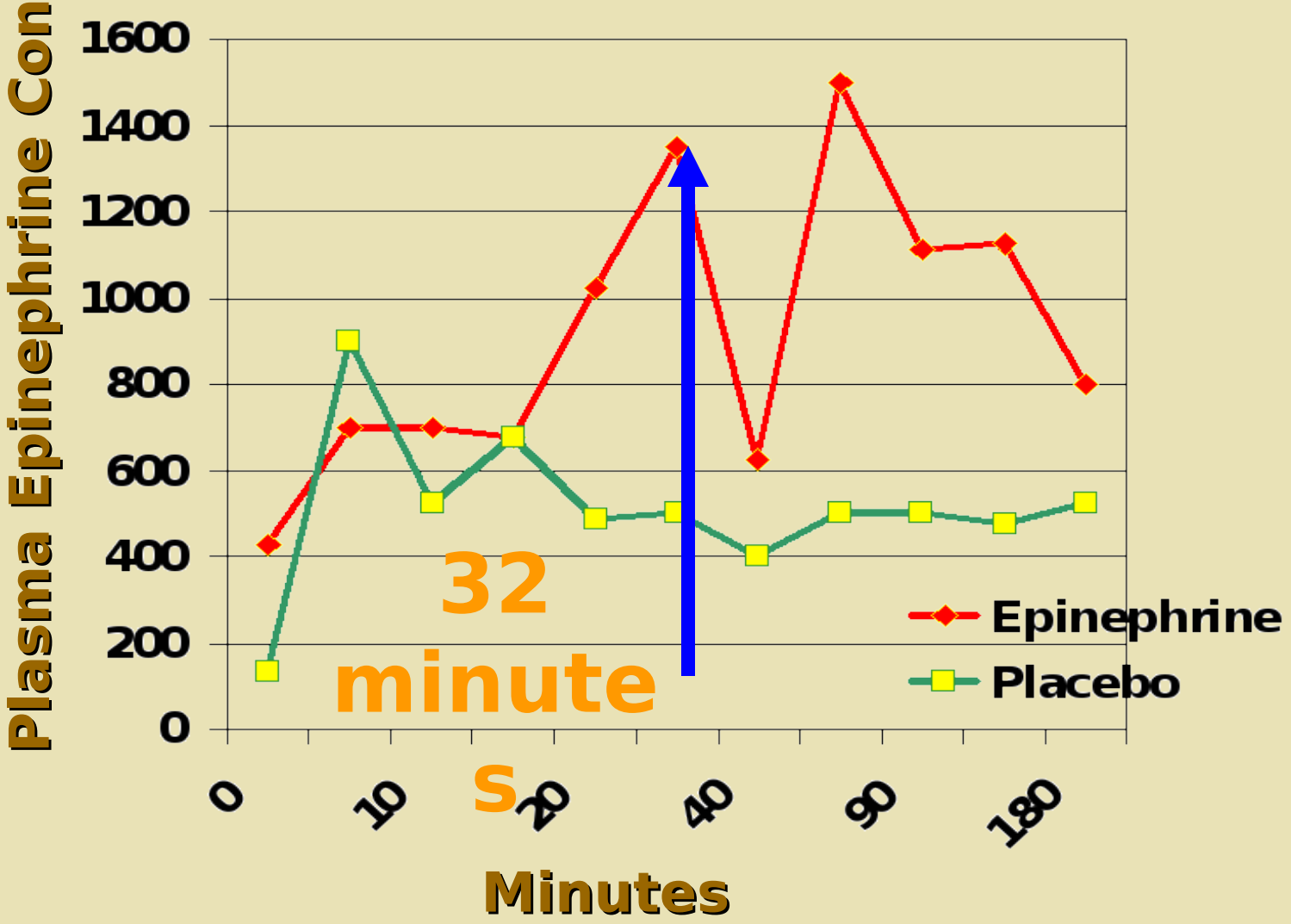
With what Device do you give it?

Can epinephrine inhalations be substituted for epinephrine injection in children at risk for systemic anaphylaxis?

- 19 asymptomatic children
- Based on the child's weight, 10, 15, or 20 epinephrine or placebo inhalations were administered
- Monitored plasma epinephrine concentrations, heart rate, blood pressure, and adverse effects

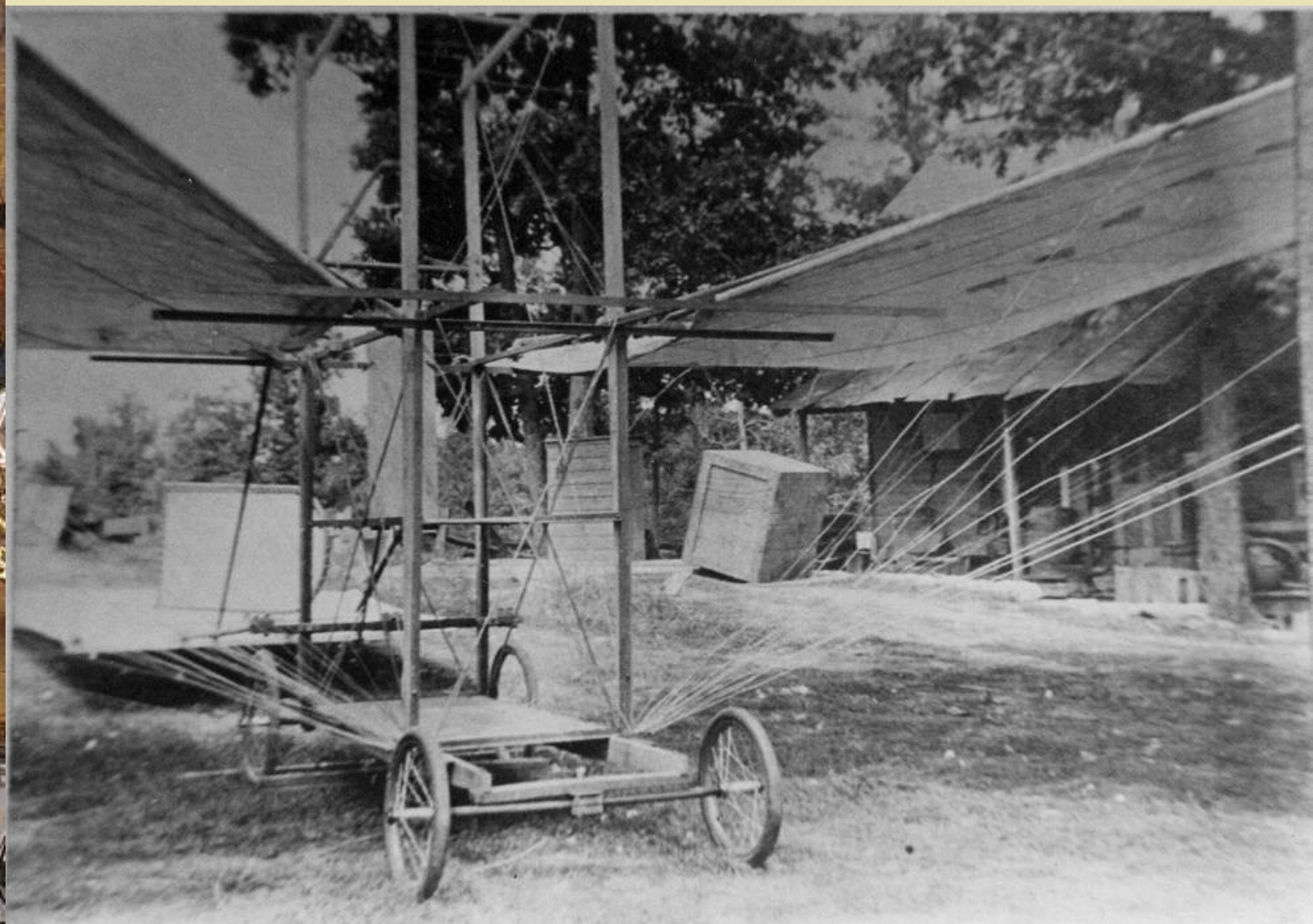
Pediatrics **2000; 106: 1040-4**

Can epinephrine inhalations be substituted for epinephrine injection in children at risk for systemic anaphylaxis?



Pediatrics 2000;

OK, that doesn't work...

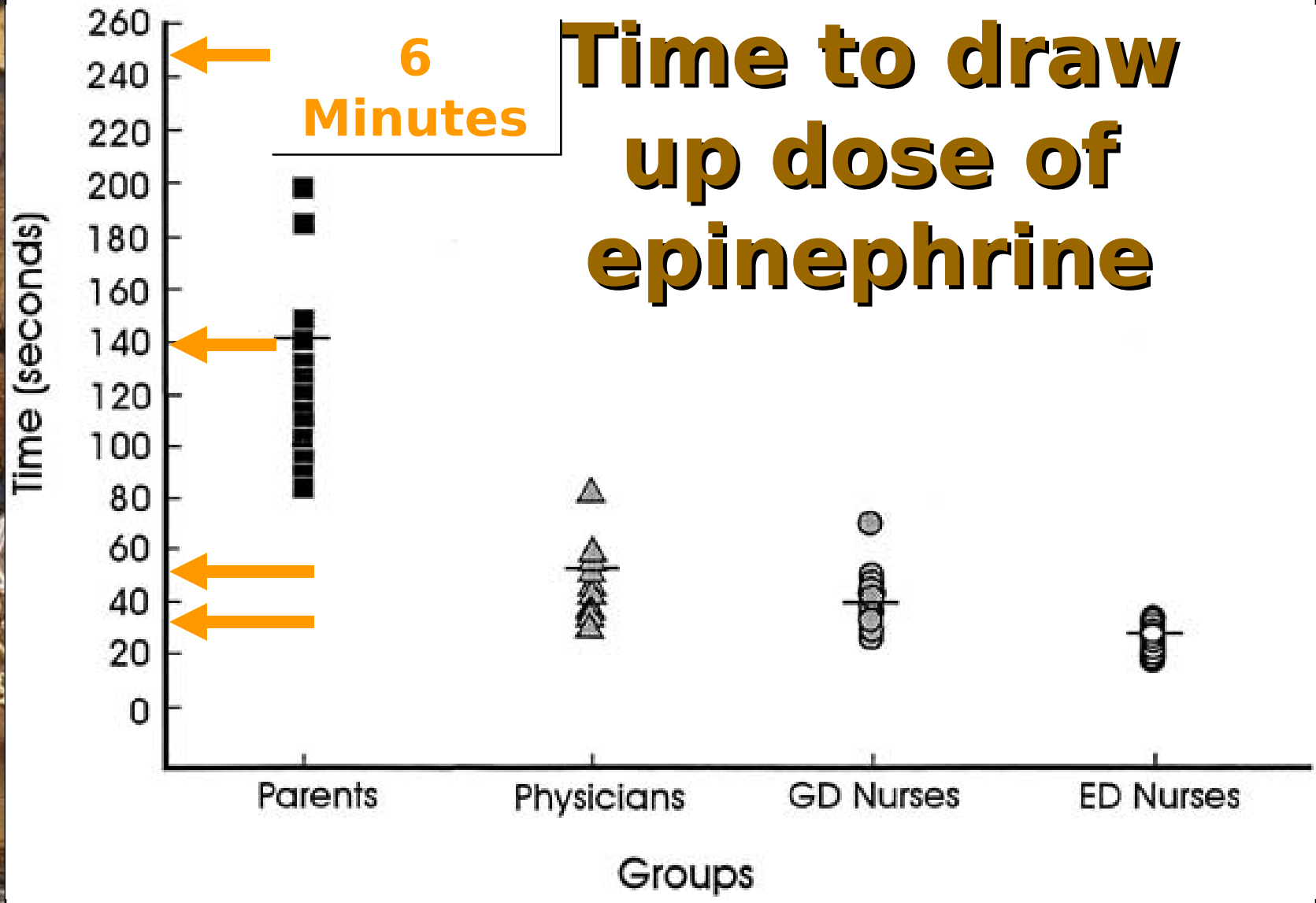


DOSETTE® AMPUL
EPINEPHRINE
1mg/ml

Instructions for Injection from an Ampule

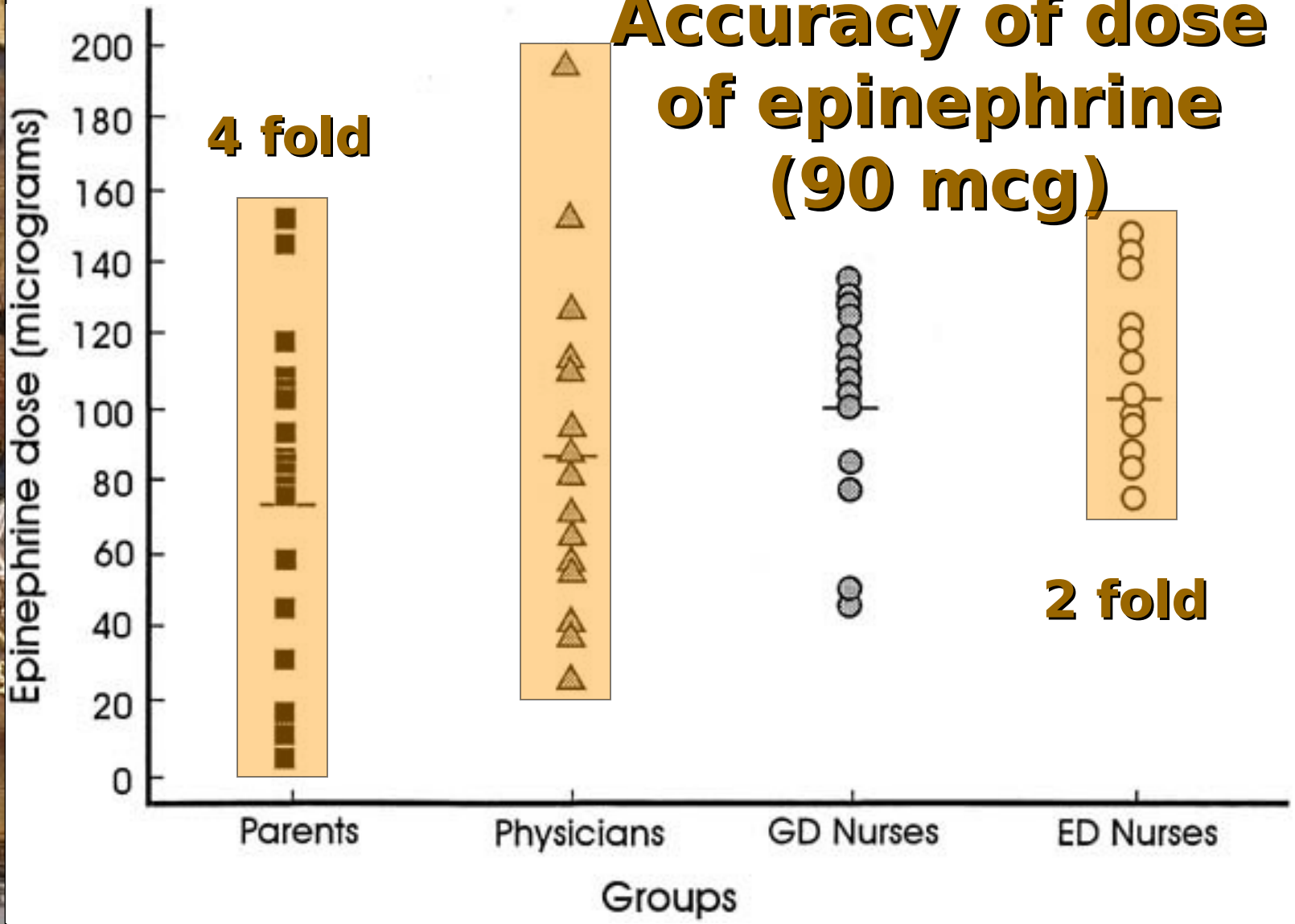
1. Tap epinephrine ampule to make sure liquid is at the bottom
2. Snap top off ampule
3. Remove sterile syringe with attached needle from package
4. Take cap off needle
5. Put needle tip in epinephrine and pull up liquid
6. Hold needle point up and syringe down, then tap air out of syringe
7. Measure the epinephrine dose of 0.09 mL
8. Inject the epinephrine.

Time to draw up dose of epinephrine



*J Allergy Clin Immunol 2001;108:1040-4

Accuracy of dose of epinephrine (90 mcg)



*J Allergy Clin Immunol 2001;108:1040-4

Epinephrine for the out-of-hospital treatment of anaphylaxis in infants: Is the ampule/syringe/needle method practical?*

- Most parents (and *physicians*) are unable to draw up an infant dose of epinephrine rapidly or accurately

*J Allergy Clin Immunol 2001;108:1040-4

PATIENT DIRECTIONS FOR USE
IMPORTANT
Hollister Stier
ANAKIT
ANAPHYLAXIS EMERGENCY TREATMENT KIT
EPINEPHRINE
PDI
Alcohol
Prep
Pad
SMALL

Twinject

Twinject
auto-injector
DEMONSTRATOR
CONTAINS NO NEEDLE OR EPINEPHRINE
See Enclosed
Lot: D0303001

TWIST AND PULL TO OPEN
FOR PRACTICE ONLY - REUSABLE
Twinject
auto-injector
Twinject
auto-injector
DEMONSTRATOR
Lot:

Side One

PATIENT DIRECTIONS

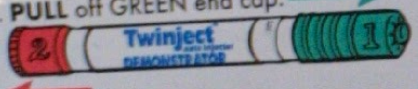
Step 1 – Make Sure That The Medicine Is Ready When You Need It

Note: The Twinject™ Demonstrator does not contain medicine.

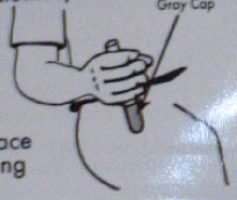
Simulate looking at the medicine in the Twinject™. An actual Twinject™ auto-injector would not be used if it has particles, is pinkish or slightly yellow in color, or has passed its expiration date.

Step 2 – First Dose

1. **PULL** off GREEN end cap.



2. **PULL** off RED end cap.
3. Put the GRAY cap against the middle of the outer side of your thigh (upper leg) as shown. (If this were a real auto-injector, it could go through clothes).



4. Press down firmly. (If this were a real auto-injector, the unit would now activate.) Hold the demonstrator in place while slowly counting to 10.
5. Remove the Twinject™ Demonstrator from your skin. Get ready for the second dose.
6. **In the case of a real emergency, get emergency medical help right away.**

(Directions continue on reverse side)

Instructions similar to these are found attached to the barrel of your Twinject™ auto-injector.

Twinject™ auto-injector DEMONSTRATOR

DEMONSTRATOR DEMONSTRATOR

CONTAINS NO NEEDLE OR EPINEPHRINE FOR PRACTICE ONLY - REUSABLE

IMPORTANT: Read and become familiar with these instructions prior to use.

Peel Here, then Press To Open

TWIST AND PULL TO OPEN FOR PRACTICE ONLY - REUSABLE Twinject™

SIMULATED SYRINGE FOR DEMONSTRATION ONLY

Using Twinject® Does Not Eliminate The Need For Prompt Emergency Medical Attention.

Side One
PATIENT DIRECTIONS

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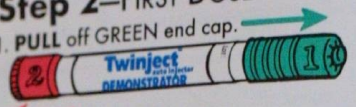

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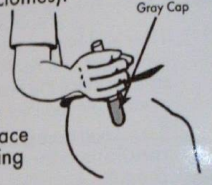

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DEMONSTRATOR DEMONSTRATOR

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IMPORTANT: Read and become familiar with these instructions prior to use.

IMPORTANT: Read and become familiar

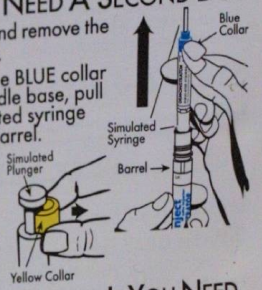
Hollister-Stier Laboratories LLC
Spokane, WA 99207 USA

PROCEED WITH STEPS 3 - 6

Side Two
PATIENT DIRECTIONS

Step 3—Get Ready In Case You Need A Second Dose

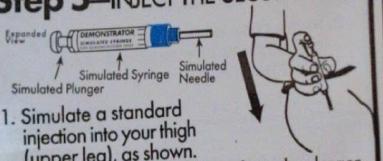
1. Unscrew and remove the GRAY cap.
2. Holding the BLUE collar at the needle base, pull the simulated syringe from the barrel.
3. Slide the YELLOW collar off the simulated plunger.



Step 4—Decide If You Need A Second Dose

1. If this had been a real emergency and your symptoms had not improved after about 10 minutes since the first injection, you would need a second injection. Begin Step 5.
2. If a second dose is not needed, **the unused medicine is thrown away as directed in Step 6.**

Step 5—Inject The Second Dose



1. Simulate a standard injection into your thigh (upper leg), as shown.
2. Simulate manually pushing down the plunger all the way.
3. Remove the simulated syringe from your skin.
4. In the case of a real emergency, get emergency medical help right away.

Step 6—Proper Disposal

1. Refer to the instructions accompanying your Twinject™ auto-injector for proper disposal guidelines.
2. The Twinject™ Demonstrator is reusable. To reassemble, put the YELLOW collar back onto the simulated plunger, replace the simulated syringe into the barrel, screw the GRAY cap on, and reapply the GREEN and RED caps

Side Two

PATIENT DIRECTIONS

Step 3—Get Ready In Case You Need A Second Dose

1. Unscrew and remove the GRAY cap.
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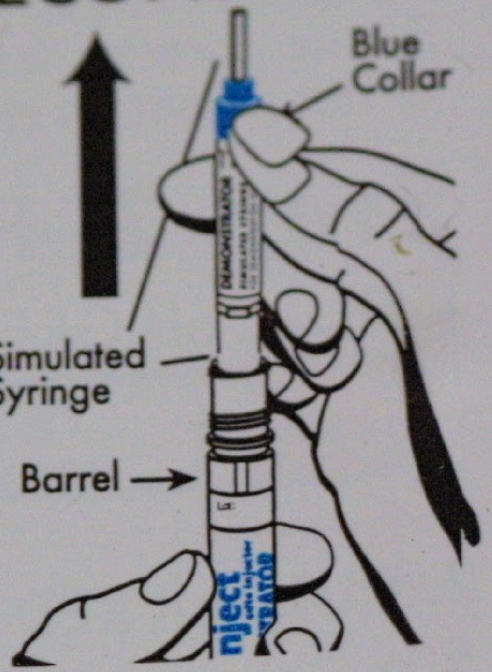

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Side One

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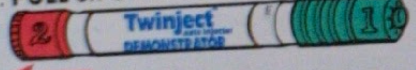

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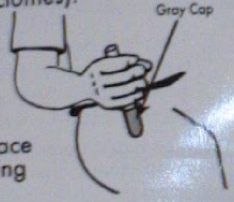

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(Directions continue on reverse side)

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Twinject™ auto-injector DEMONSTRATOR

DEMONSTRATOR DEMONSTRATOR

CONTAINS NO NEEDLE OR EPINEPHRINE FOR PRACTICE ONLY - REUSABLE

IMPORTANT: Read and become familiar with these instructions prior to use.

Peel Here, then Press To Activate

TWIST AND PULL TO OPEN
FOR PRACTICE ONLY - REUSABLE™
Twinject

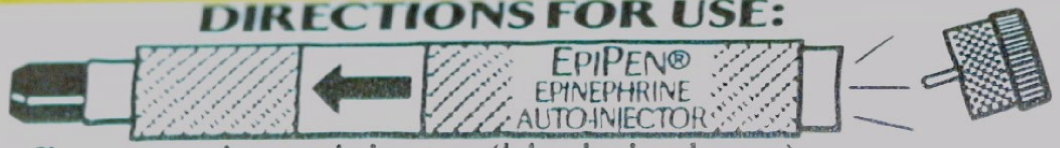
When you feel like this...

Keep It Simple!

1. **Form fist around auto-injector**
2. **Pull out the gray safety cap**
3. **Place the black tip near the outer thigh**
4. **Jab firmly into thigh**
5. **Hold in place for 10 seconds**

DO NOT REFRIGERATE. CONTAINS NO LATEX.

DIRECTIONS FOR USE:



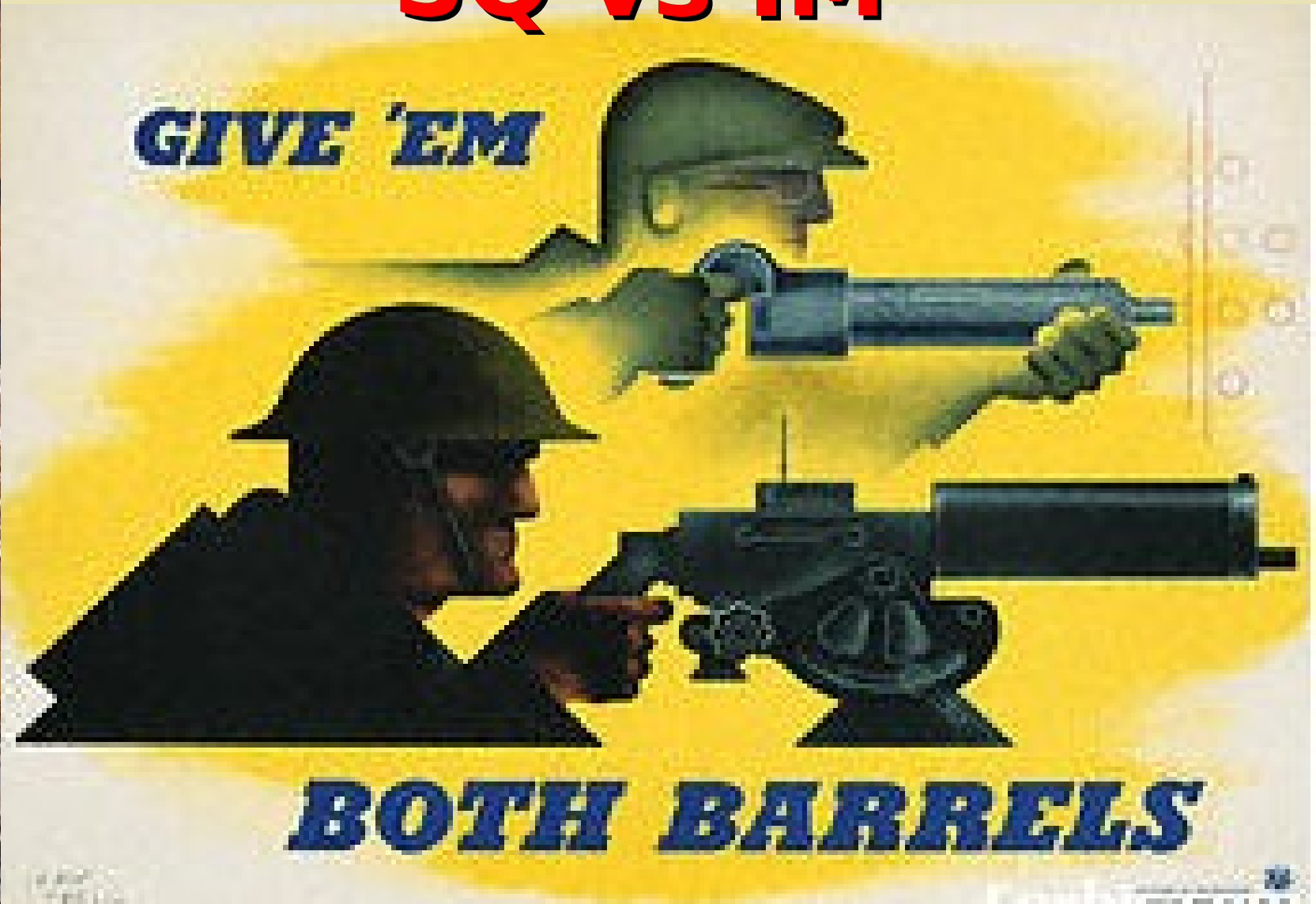
1. Form fist around auto-injector (black tip down)
2. With your other hand, pull off gray cap.
3. Hold black tip near outer thigh.
4. Swing and **jab firmly** into outer thigh so auto-injector is perpendicular (at 90° angle) to thigh.
5. Hold firmly in thigh for several seconds.

With what Device do you give it?

But Remember…**Give Two**

How to Give Epinephrine?

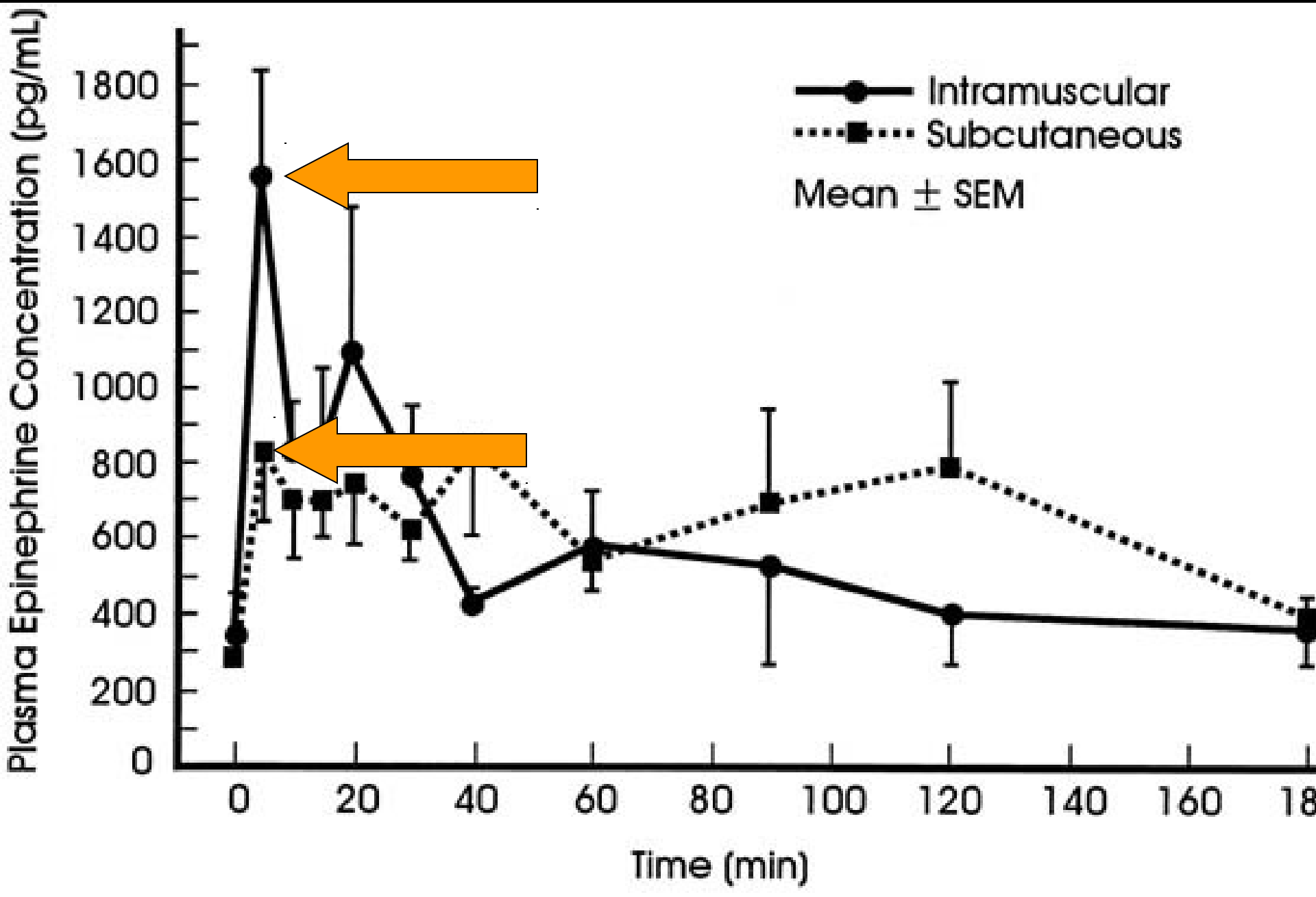
SQ vs IM



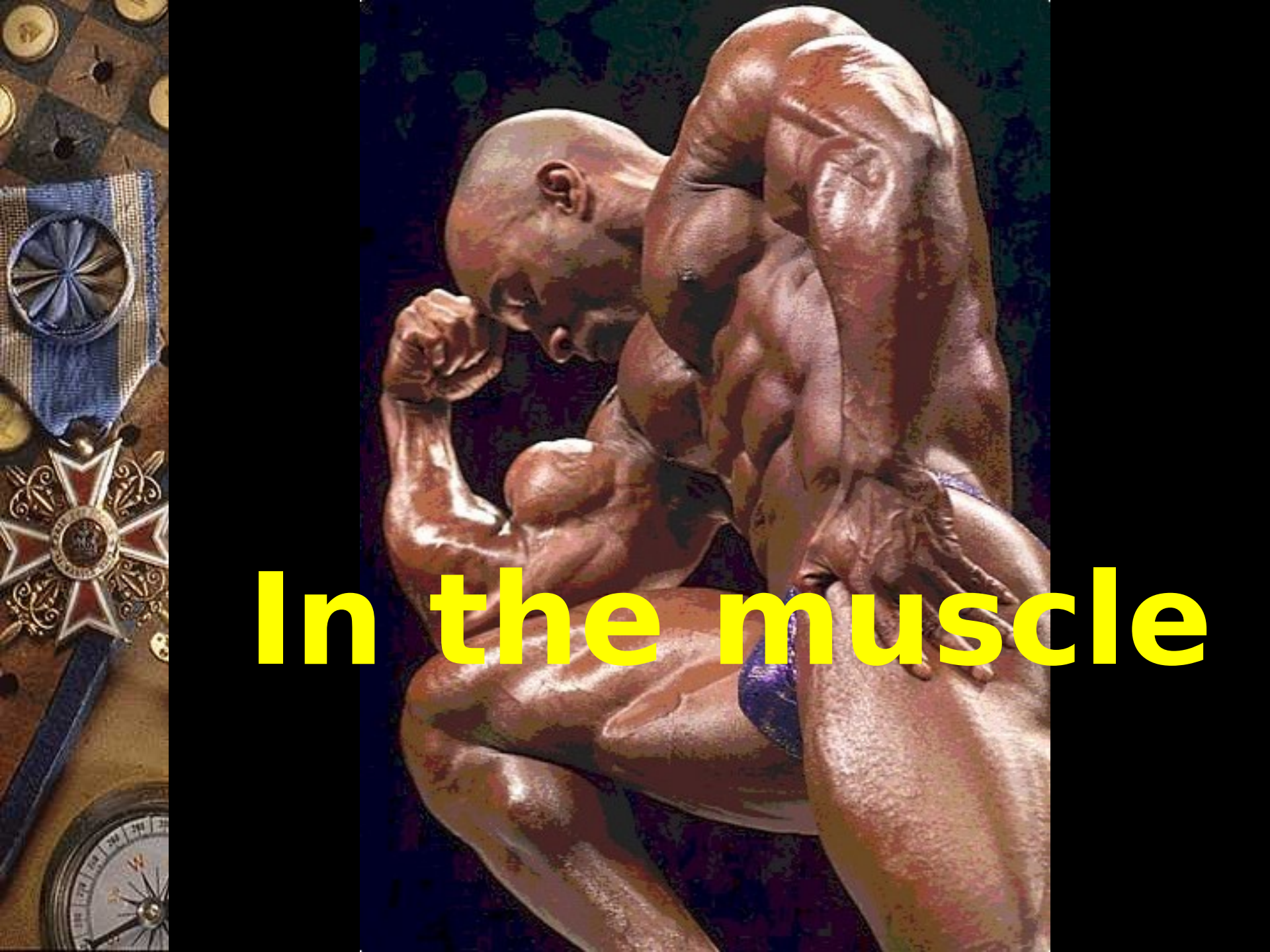
Epinephrine Absorption in Children with a History of Anaphylaxis*

- 17 children
- 9: Epi 0.01 mg/kg SQ
- 8: Epi 0.3 mg IM from EpiPen
- Monitored:
  - Plasma epinephrine concentration
  - Heart rate
  - Blood pressure
  - Adverse effects

***JACI 1998;101:33-7**


Plasma Epinephrine Concentration (pg/mL)
1800
1600
1400
1200
1000
800
600
400
200
0
0
20
40
60
80
100
120
140
160
Time (min)
Intramuscular
Subcutaneous
Mean ± SEM

How to Give Epinephrine?

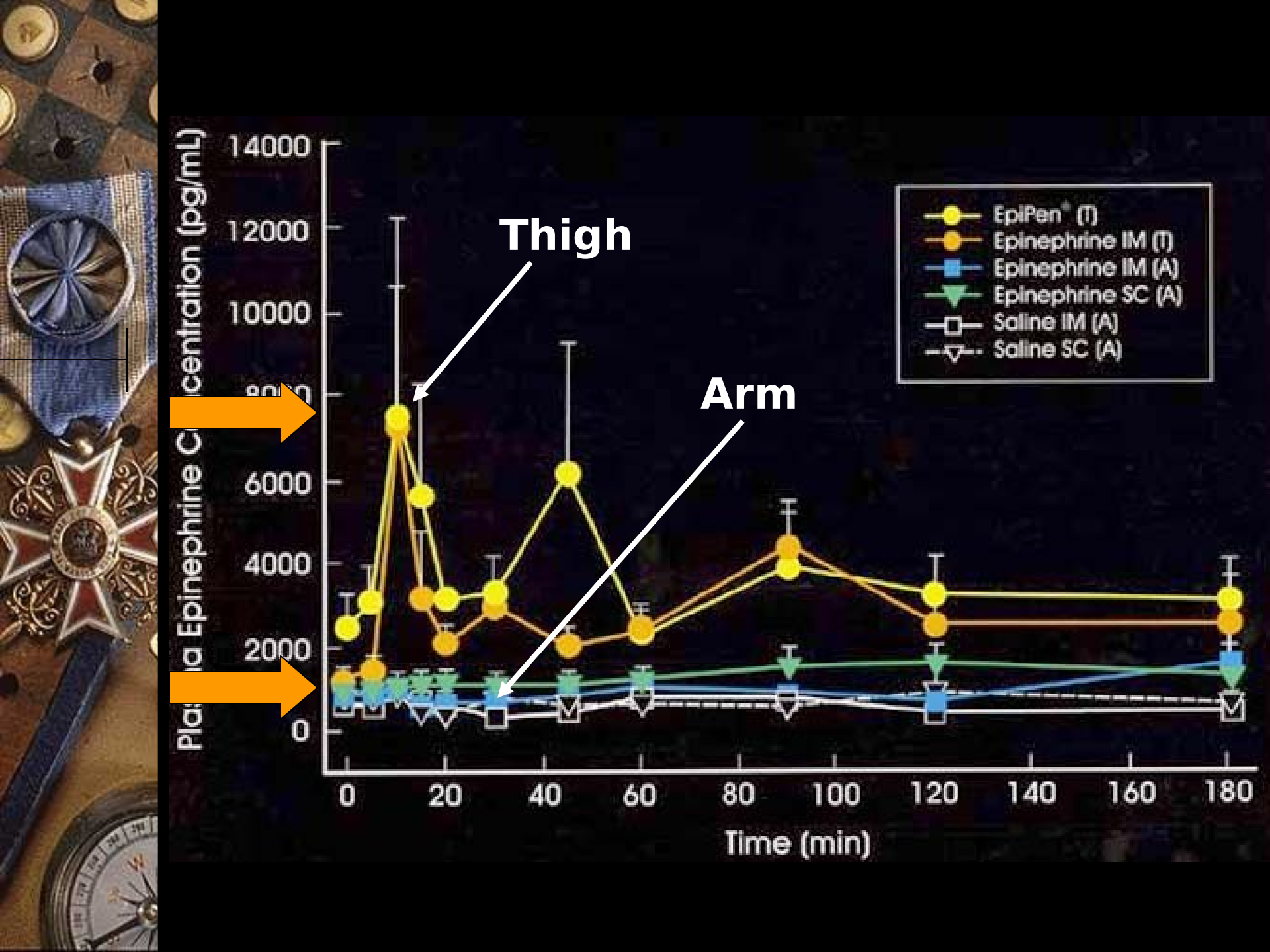

In the muscle

Which Muscle ?

Epinephrine absorption in adults: Intramuscular vs subcutaneous injection*

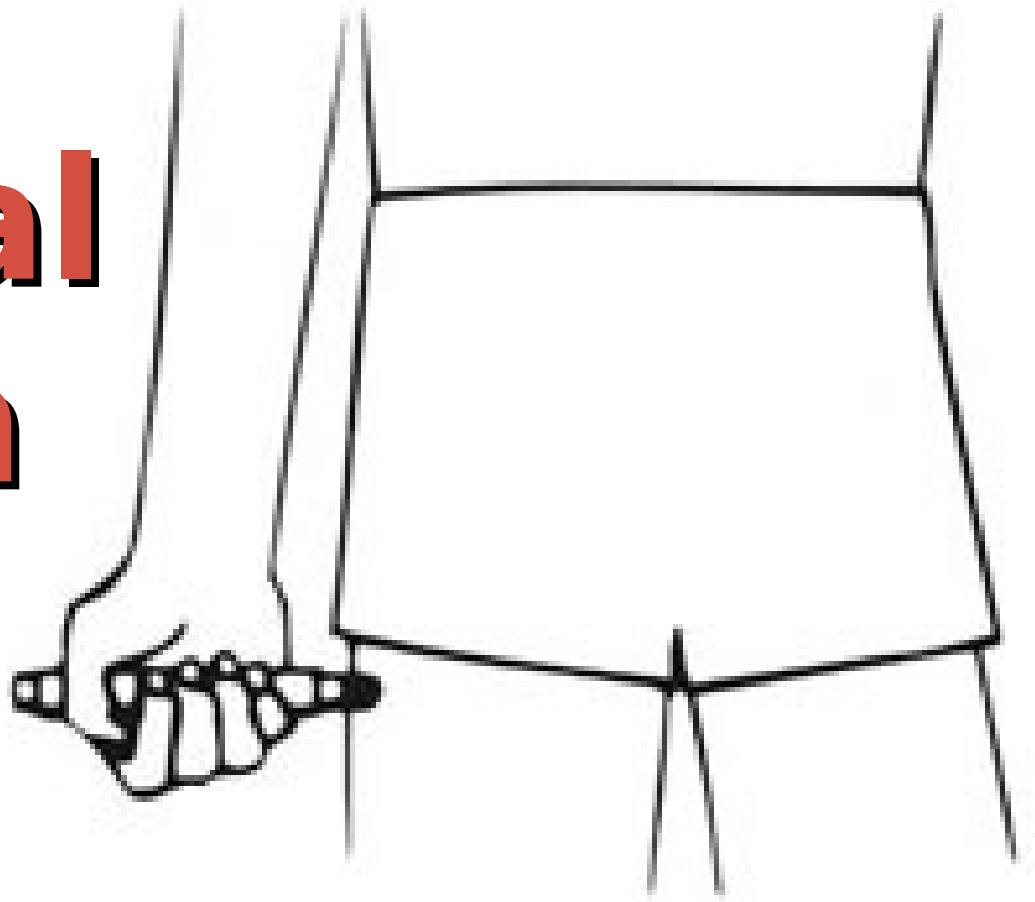
- Crossover study in healthy men age 18 to 35
- 4 injections of epinephrine 0.3 mg SQ and IM and 2 injections of saline
- I.M.: Arm vs. Thigh

***JACI 2001;108:871-3**


Thigh
Arm
EpiPen® (T)
Epinephrine IM (T)
Epinephrine IM (A)
Epinephrine SC (A)
Saline IM (A)
Saline SC (A)
14000
12000
10000
6000
4000
2000
0
0
20
40
60
80
100
120
140
160
180
Time (min)

Where
to Give Epinephrine?

Lateral Thigh



When
to Repeat Epinephrine?

When to Repeat Epinephrine?

- Position Statement: Repeat every 10-15 minutes
  - "For patients with life-threatening anaphylaxis unresponsive to initial dose of epinephrine, more frequent or higher doses may be required"
- UK Consensus Panel on emergency Guidelines and International consensus guidelines for emergency cardiovascular care: Epinephrine may judiciously be repeated as often as every **5 minutes**

JACI 1998;101:S469

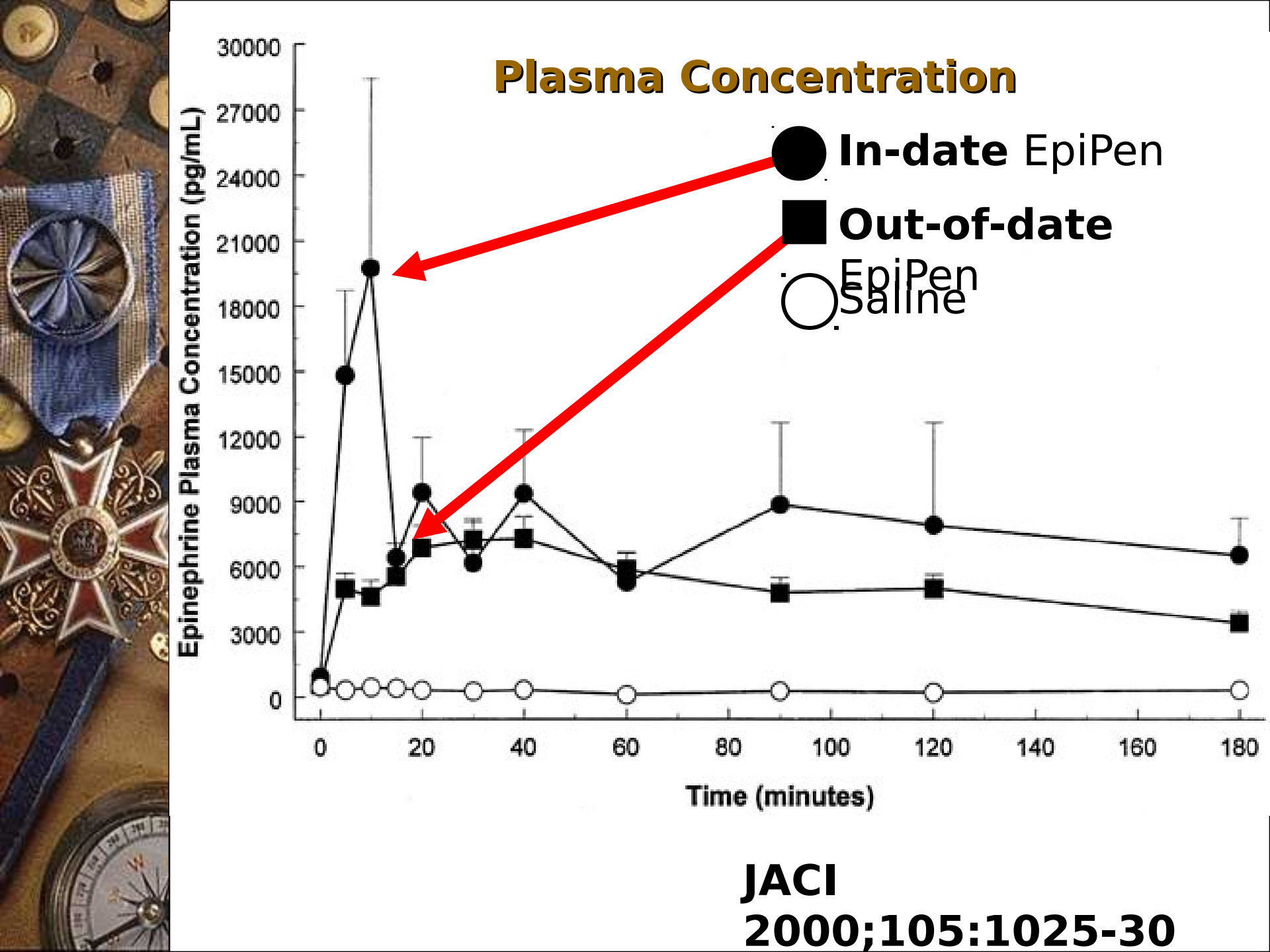
When to Change It?
(the EpiPen, that is)

LOT 2ST472
EXP MAY 04

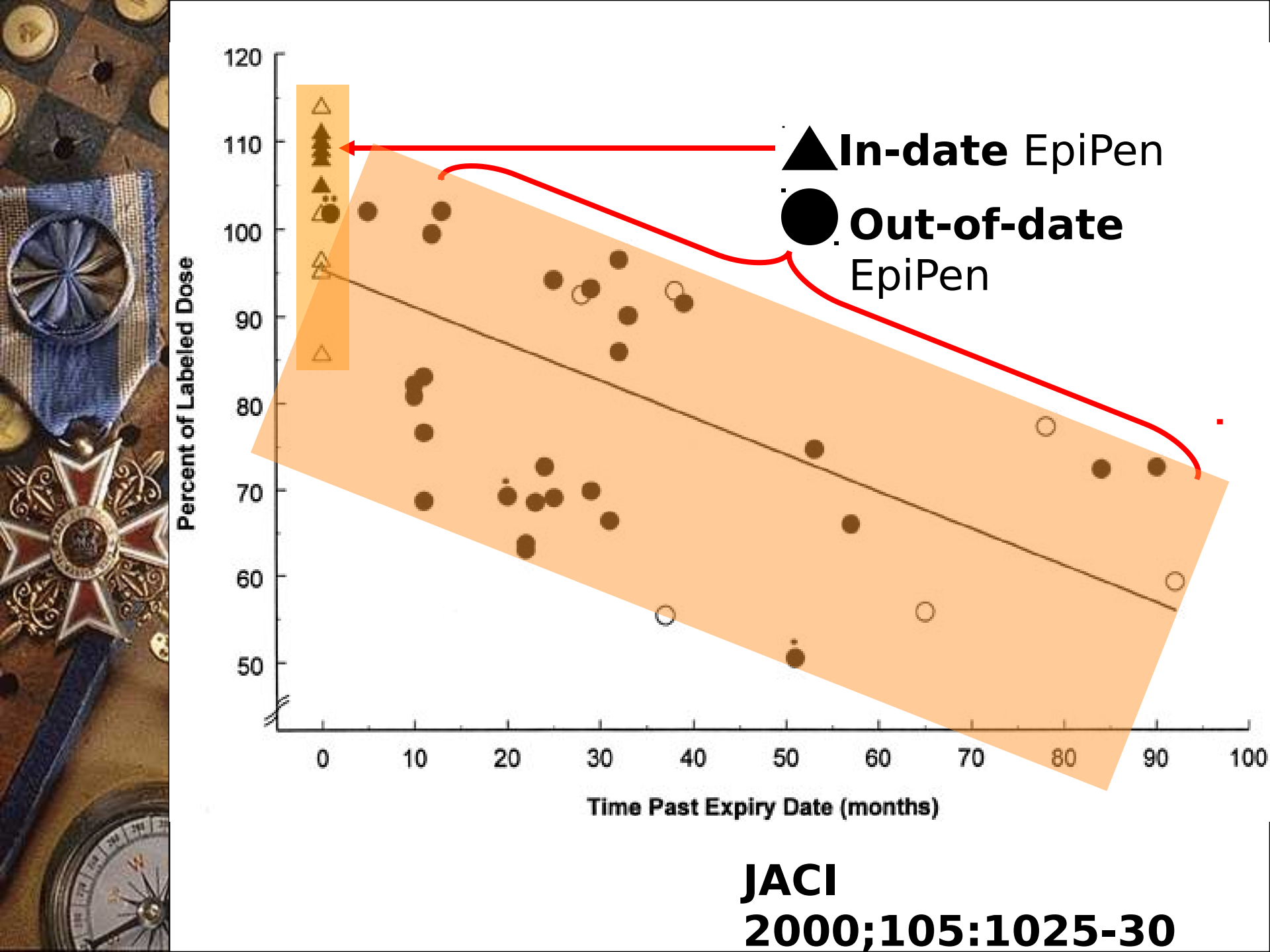
Outdated EpiPen and EpiPen Jr autoinjectors: Past their prime?*

- 28 EpiPen and 6 EpiPen Jr autoinjectors
- 1 to 90 months after the stated expiration date
- Epinephrine bioavailability assayed after injection in rabbits
- Epinephrine content measured with high pressure liquid chromatography

***JACI 2000;105:1025-30**



JACI
2000;105:1025-30



JACI 2000;105:1025-30

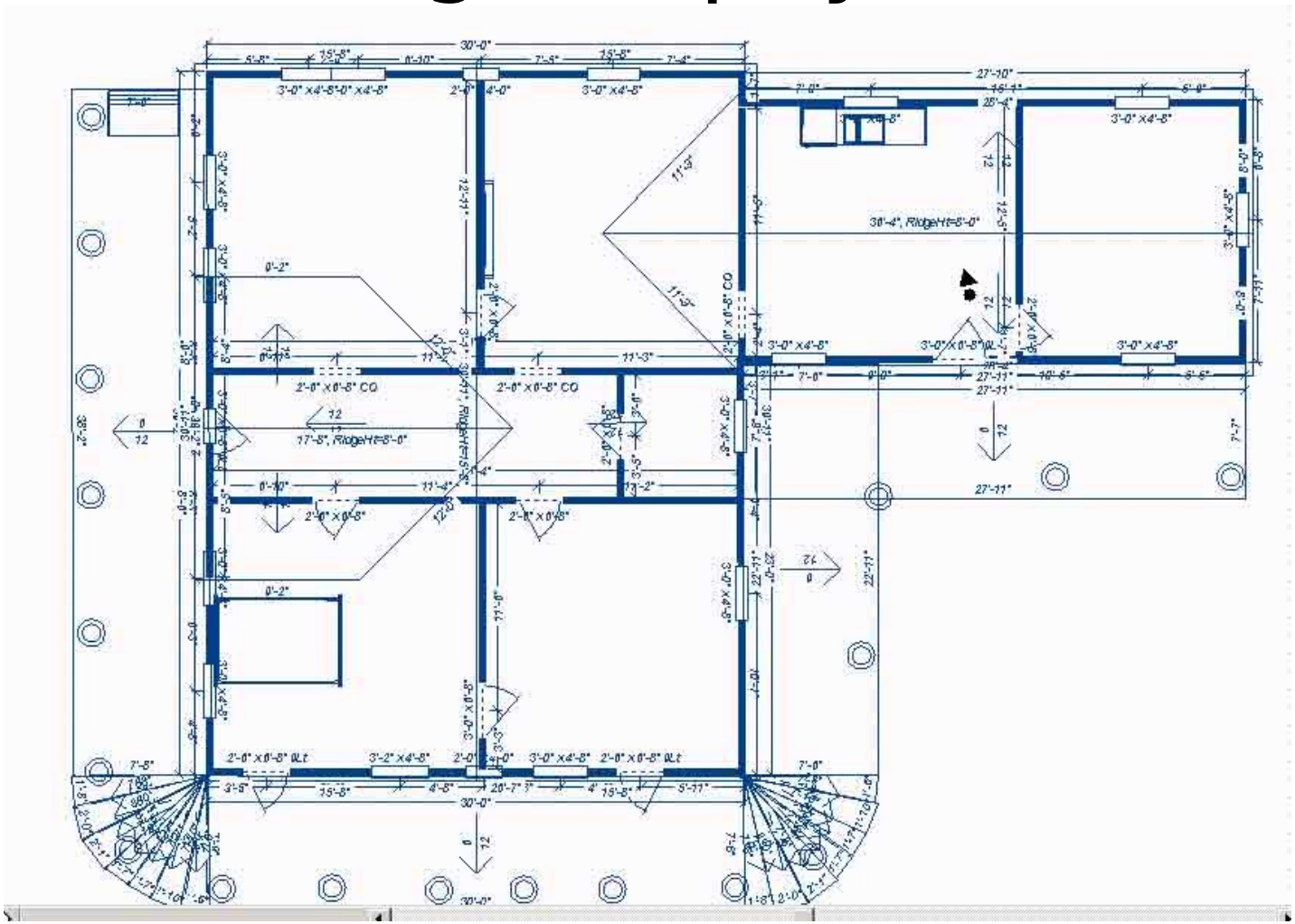
When to Change It?

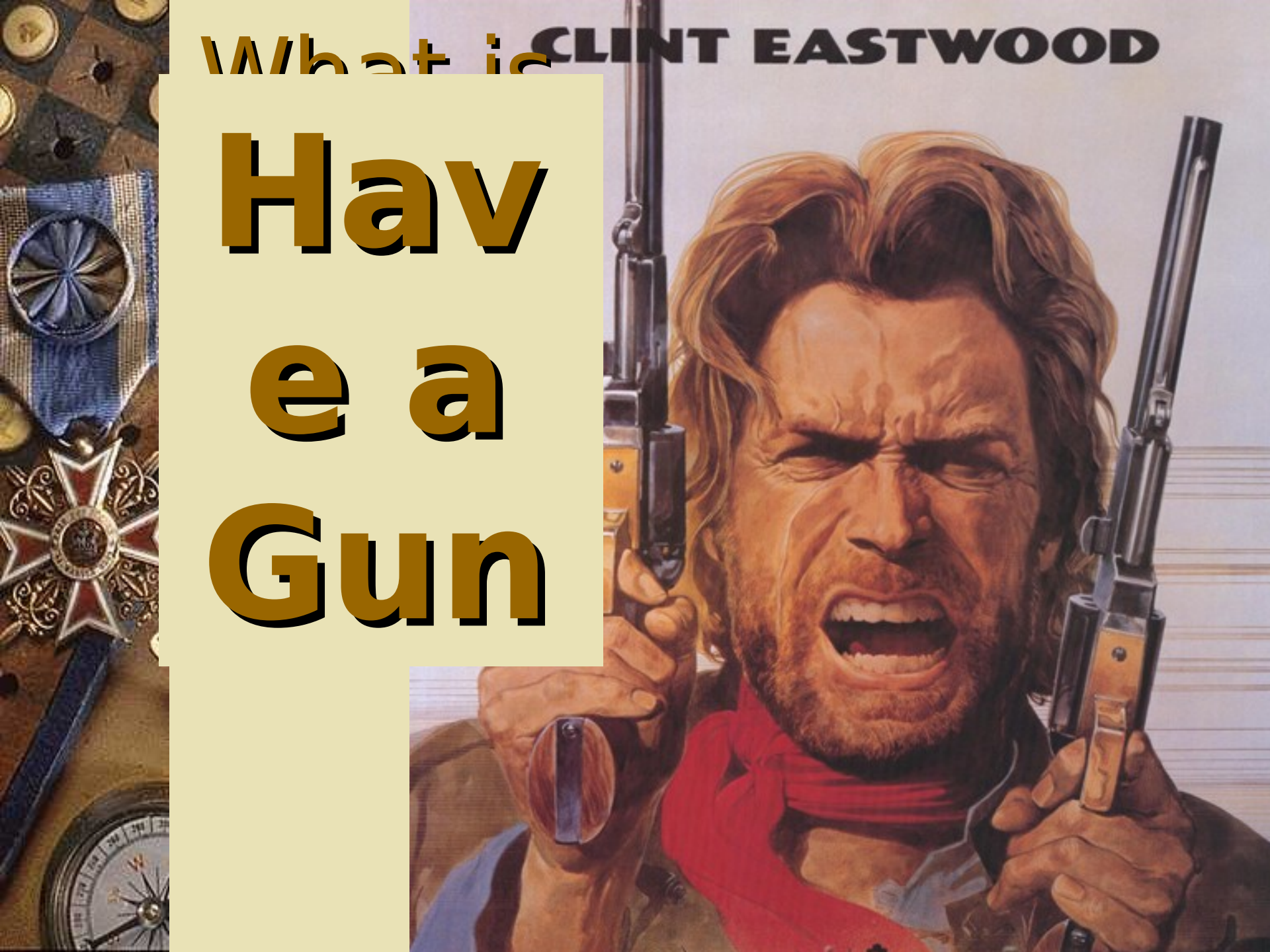
"Before the Expiration Date"

- If the only autoinjector available is an outdated one, the potential benefit of using it is greater than no epinephrine treatment at all

JACI 2000:105:1025-30

What Is Our Plan For Treating Anaphylaxis?





What is

Hav e a Gun

Epinephrine

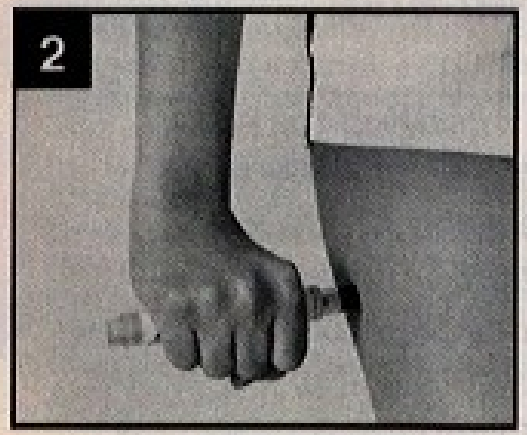
- Prescribe an EpiPen
- "Avoidance" doesn't work

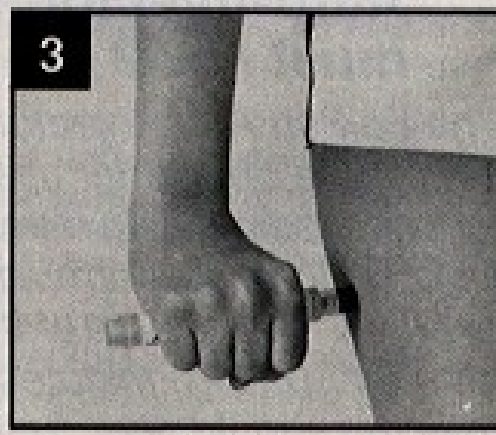
EpiPen

Educate!

Educate!

Educate!





Pat. No. 4,640,686

over the
TIP.

Do We Need to Educate ?

Anaphylaxis and epinephrine auto-injector training: Who will teach the teachers?*

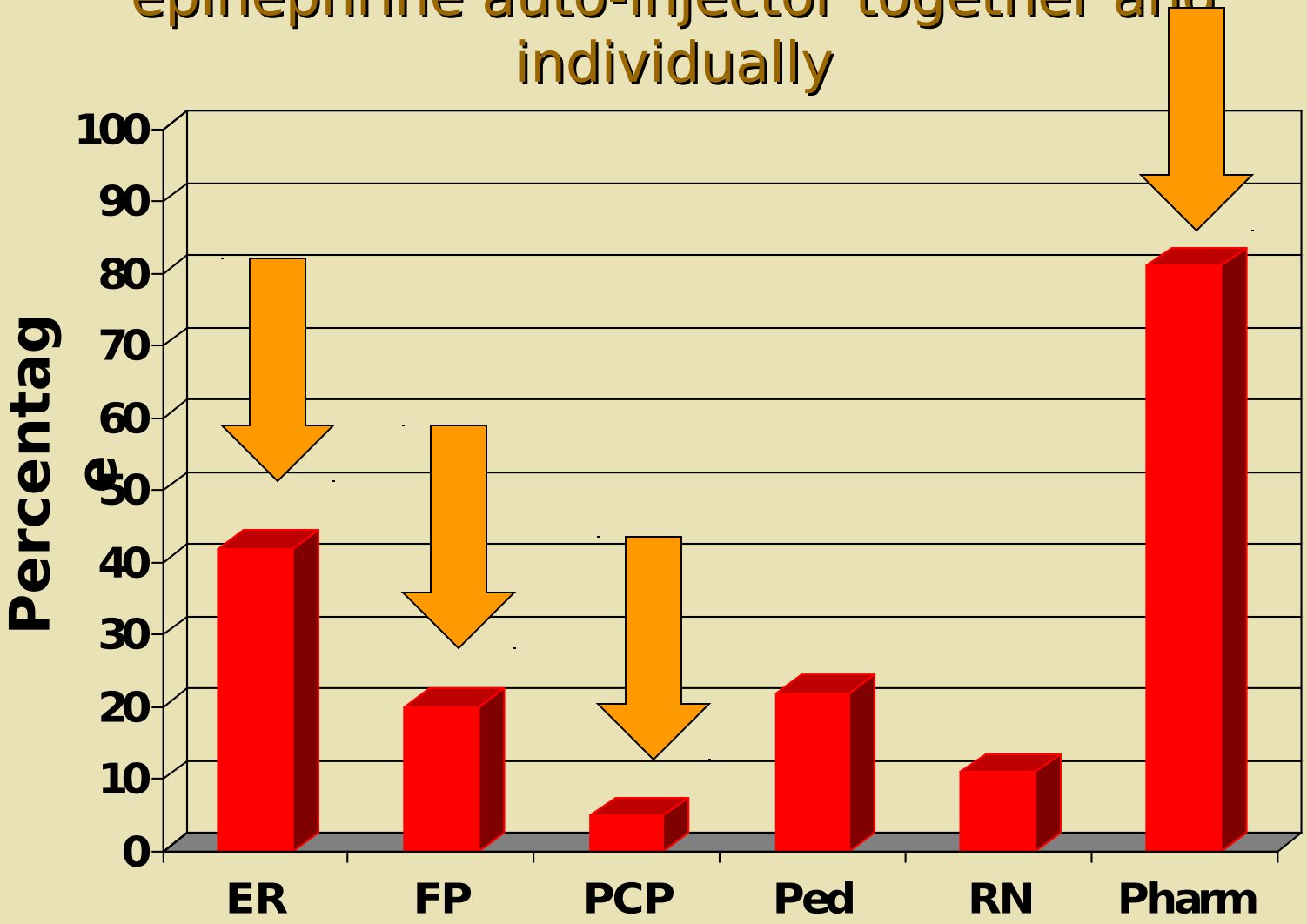
- 122 professionals
  - Emergency physicians
  - Family practitioners
  - Pediatricians
  - Pharmacists
- Perform the 3 steps for use of the epinephrine auto-injector together and individually

*J Allergy Clin Immunol 1999;103:190-3.)

Steps for use of the epinephrine auto-injector trainer device

1. Pull out the gray safety cap
2. Hold the device in the palm with the thumb covering the index finger and the black tip toward the small finger
3. Place the black tip on the outer thigh. Push hard until you hear the trainer function. Hold in place for 10 seconds

Proportion of medical personnel correctly performing the 3 steps for use of the epinephrine auto-injector together and individually



A survey of EpiPEN use in patients with a history of anaphylaxis*

- 98 patients
- Ages ranging from 18 months to 18 years

JACI 1998;102:*102:525-6

A survey of EpiPEN use in patients with a history of anaphylaxis*

90% Knew to remove the cap before the injection

78% Knew to press the Epi-PEN on the lateral thigh

37% Knew to press Epi-PEN until a clicking is heard

41% Knew to hold Epi-PEN in place for 10 seconds

53% Knew Epi-PEN can be used without removing clothes

97 % Knew there was an expiration date on Epi-PEN

JACI 1998;102:*102:525-6*

First aid anaphylaxis management in children who were prescribed an epinephrine autoinjector device (EpiPen)*

- 68 children given Epi-Pen for anaphylaxis
- Followed for 2 years
- 121 episodes of anaphylaxis
  - 1episode/patient/year

*J Allergy Clin Immunol 2000;106:

First aid anaphylaxis management in children who were prescribed an epinephrine autoinjector device (EpiPen)*

EpiPen Knowledge

- 24% parents were able to recall all steps required for the correct use of the EpiPen autoinjector device
- 50% did not remembered that the gray cap had to be removed
- 50% did not know that the device had to be held in place for 10 seconds.
- 5% parents could not recall any steps

***J Allergy Clin Immunol 2000;106:171-6**

First aid anaphylaxis management in children who were prescribed an epinephrine autoinjector device (EpiPen)*

Recognition of Anaphylaxis

- Parents could describe:
  - Skin rash
  - Shortness of breath
- Few parents could describe:
  - Upper airway obstruction (noisy breathing, hoarse voice, difficulty swallowing or talking)
  - Hypotension (loss of consciousness or collapse)

*J Allergy Clin Immunol 2000;106:171-6

First aid anaphylaxis management in children who were prescribed an epinephrine autoinjector device (EpiPen)*

Treatment of Anaphylaxis

- 40% children had an EpiPen device at school, an anaphylaxis action plan, documented consent, and a school staff member trained to use the device
- 12% used EpiPen
  - Those children who used the EpiPen were less likely to be given epinephrine in the hospital or to require subsequent hospital admission

*J Allergy Clin Immunol 2000;106:171-6

Oh, Yeah

Epinephrine

- Medic-Alert

What Not to Give

β-Blockers in Anaphylaxis

- Block the β1 and β2 anti-anaphylactic actions of epinephrine
- Cause unopposed α-adrenergic effects of epinephrine
  - Coronary artery constriction
  - Exagerated systemic pressor effects
- Caused unopposed reflex vagotonic effects
- Augment mediator release
- Bronchoconstriction
- Bradycardia

β-Blockers in Anaphylaxis

- Patients on Immunotherapy have **3-7** times the incidence of anaphylaxis
- Anaphylaxis is more **severe**
- **9** times more likely to be hospitalized
- **3** times more likely for anaphylaxis to follow a protracted course

1. Annals of Allergy 1986;56:331

2. Annals of Int Med 1991 115:270-276

β-Blockers in Anaphylaxis

- If possible β-Blockers should not be given to patients
  - On Immunotherapy
  - History of anaphylaxis from any other cause
    - Foods
    - Venoms
    - Idiopathic
    - Exercise induced
    - Drugs

What to Do When You Gave What You Shouldn't Have Given

Therapy of Anaphylaxis in Patients on β-Blockers

- **Epinephrine**
  - May require much higher or repeated dosages
  - Same with Dopamine

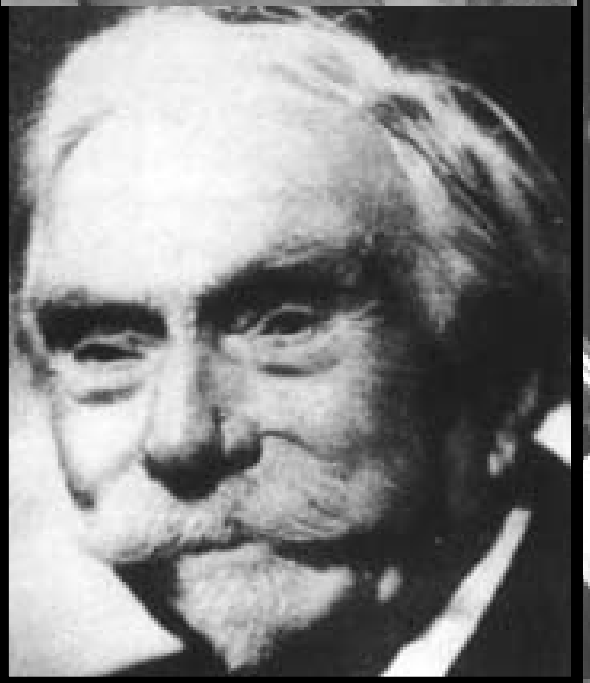
Therapy of Anaphylaxis in Patients on β-Blockers

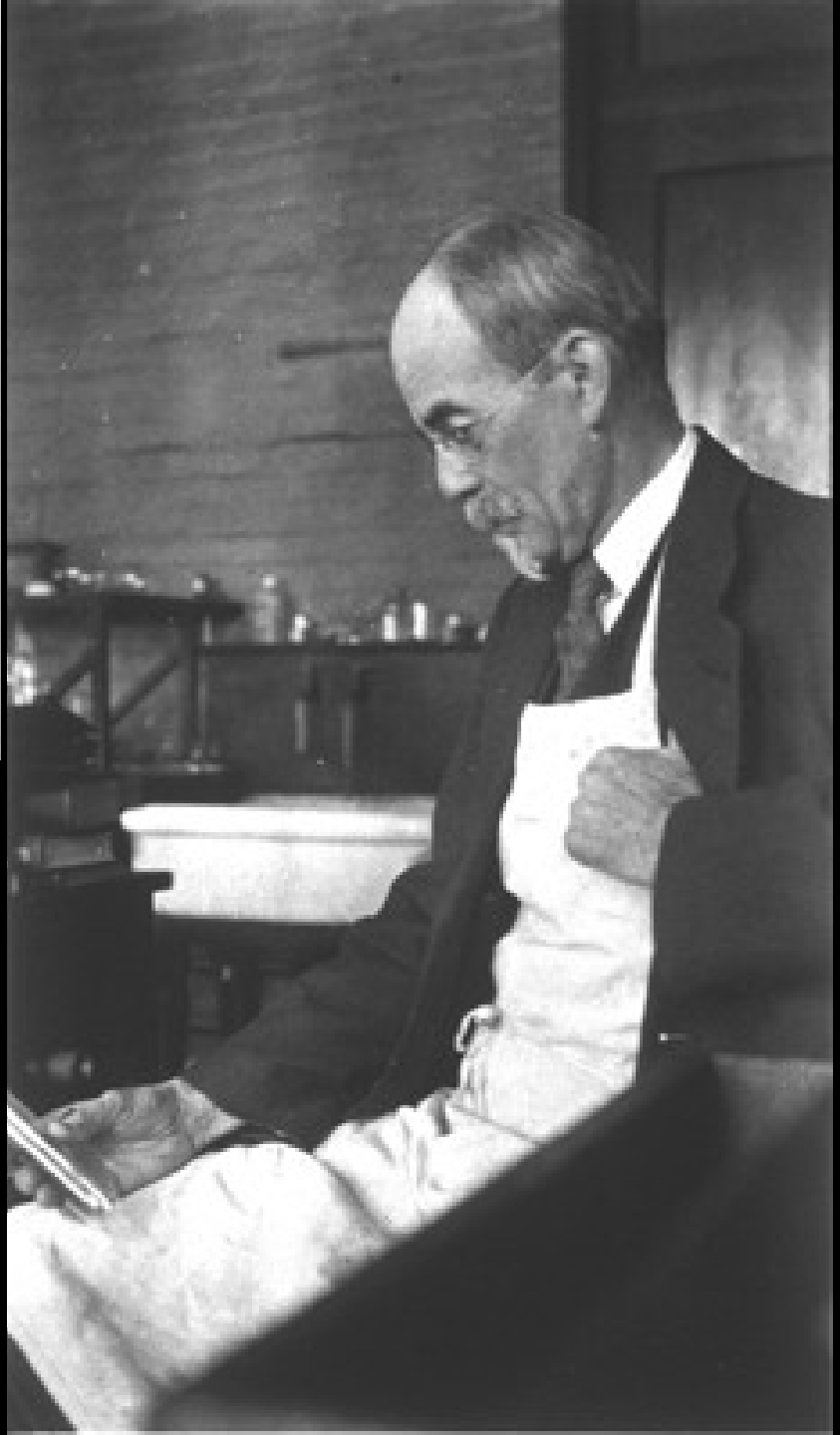
- H1 blockers
- H2 blockers (Ranitidine)
  - **NOT** Cimetadine (decreases metabolism of β-blockers)
- Atropine
  - Heart Block
  - Bronchospasm
- IV Glucagon
  - Direct action on cardiac cAMP
  - Effective in shock unresponsive to β-agonists

When to Refer to an Allergist?

When to Refer to an Allergist for Anaphylaxis

- The diagnosis is in doubt
- Help is needed for testing, identifying, or management of IgE mediated reactions
- Candidate for Immunotherapy
- Complicated or difficult cases





What do all these products have in common?
Cherries
Cherries
Cherries

They all contain cochineal...

What is cochineal (carmine dye)?

- Cochineal is a traditional red dye obtained from a scale insect, *Dactylopius coccus,* that lives its life sucking on prickly pear cacti

Carmine Dye Allergies

- Potent airborne allergen
- Rate of sensitization: in factory workers was **41.6%***
- Occupational asthma: **8.3%**
- Urticaria, angioedema and anaphylaxis after ingesting food, candy, beverages containing carmine

- What is the most important asthma risk factor in American inner-city homes?

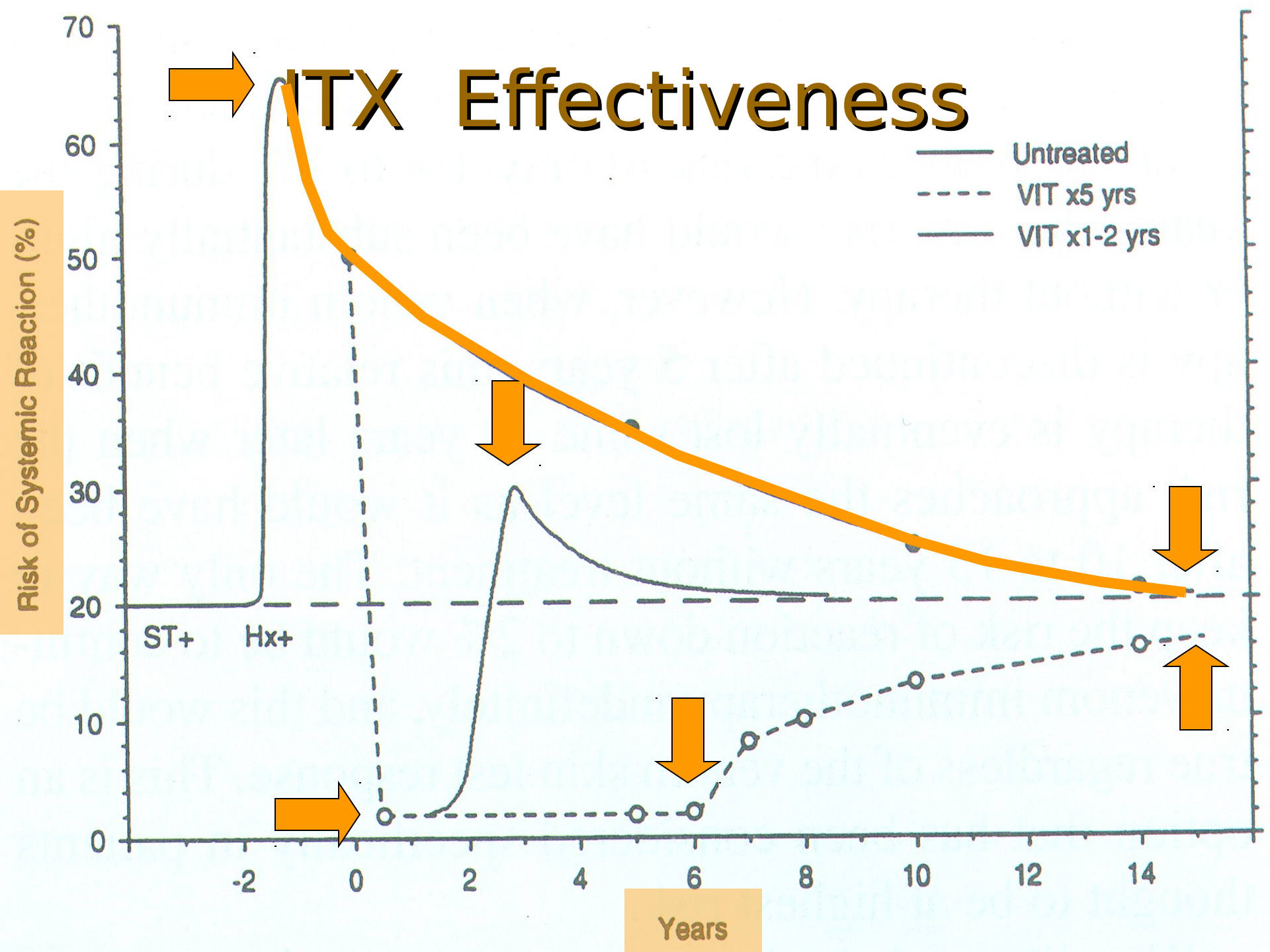
- Cockroach sensitization

- What part of cockroach contains the allergen?

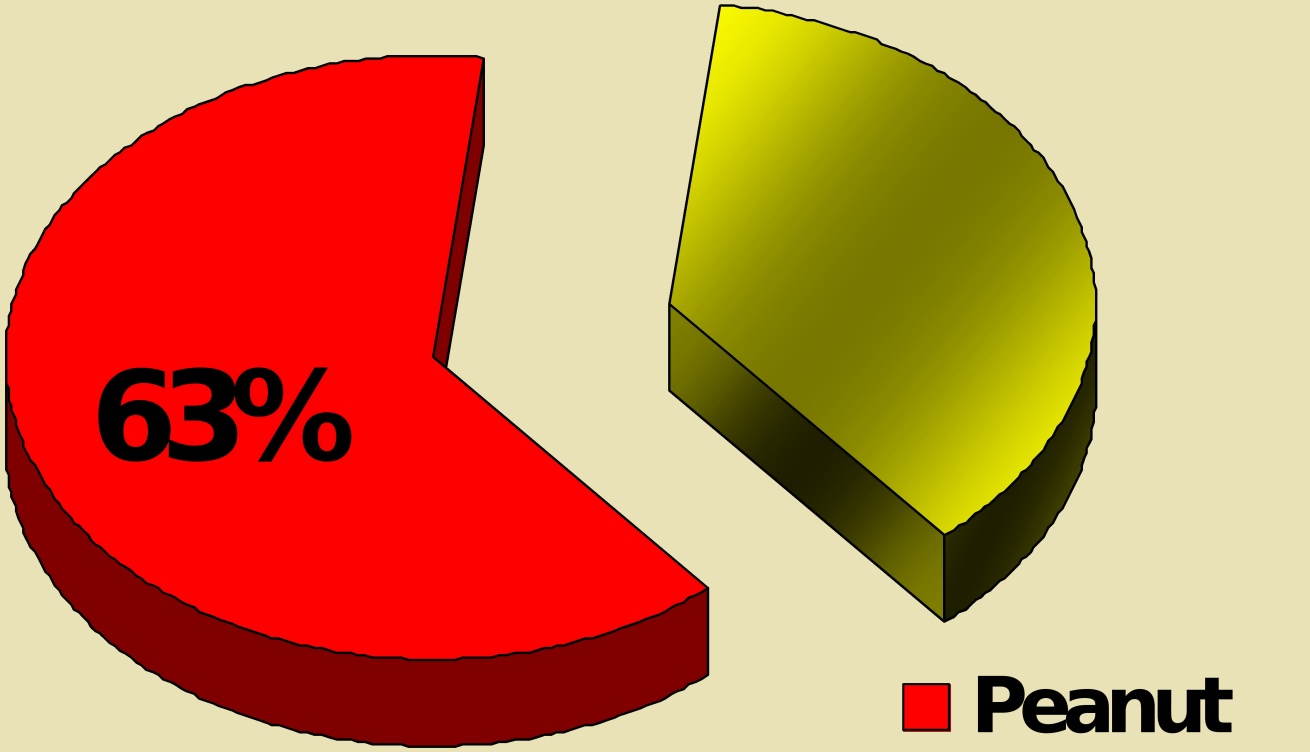
Do cockroaches like beer?

They have shown a marked attraction to alcoholic beverages, especially beer

ITX Effectiveness



Deaths From Food Anaphylaxis*



*_JACI_ 2001;107:191-3